BONE AGE ASSESSMENT USING HAND AND CLAVICLE X-RAY IMAGES

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Abstrak

Penilaian Umur Tulang (BAA) adalah satu kaedah untuk menilai tahap kematangan rangka untuk menganggar umur sebenar seseorang. Ia biasanya dilakukan secara manual dengan membandingkan imej sinar X-ray pergelangan tangan kiri dengan atlas, yang mengandungi koleksi imej X-ray orang-orang yang dikenali dalam prosedur klinikal. Kaedah manual adalah berdasarkan kepada menganalisis kawasan khas tulang tangan atau keseluruhan imej tulang tersebut. Kedua-dua pendekatan terdedah kepada kebolehubahan pemerhatian, memakan masa, dan keputusan yang dibuat mengenai umur tulang adalah subjektif. Oleh yang demikian, terdapat keperluan mendesak untuk membangunkan kaedah automatik untuk penilaian umur tulang. Kajian ini bertujuan untuk membangunkan kaedah berautomatan untuk Penilaian Umur Tulang dengan menggunakan tulang tangan dan selangka. Kajian kami mencadangkan satu kaedah baru untuk penilaian tulang dengan teknik menggunakan histogram bagi imej X-ray. Teknik ini menunjukkan satu proses pemprosesan imej baru yang depat mengatasi masalah segmentasi imej, dan sistem kami juga boleh menghapuskan masalah semasa BAA iaitu ketidaktepatan penilaian apabila BAA dibuat atas mereka yang mempunyai kecacatan dalam tangan, pertambulian tangan yang tidak normal. Teknik ini juga boleh mengatasi masalah menangani imej tangan yang noisy dengan manggunakan imej tulang selangka. Soalselidik kajian digunakan sebagai sebahagian daripada kaedah penyelidikan untuk mengenalpasti kaedah BAA yang digunakan oleh ahli radiologi, Pusat Perubatan Universiti Malaya (PPUM) dan untuk mengumpul kehendak-kehendak pengguna untak membangunkan sistem BAA berautomatan. Sistem ini, yang digelarkan BAASHC, dinilaikan dari segi prestasinya dan dari segi penerimaannya, pengguna dengan menggunakan soalselidik SUMI. Keputusan penilaian perisian menunjukkan bahawa sistem kami boleh dipercayai ketepatan yang tinggi untuk penilaian umur tulang. Pada

keseluruhannya BAASHC bukan sahaja, tetapi juga berguna untuk pakar radiologi dan doktor dalam amalan klinikal seharian bermanfaat untuk kegunaan dalam siasatan forensik.

ABSTRACT

Bone age assessment (BAA) is a method for evaluating the level of skeletal maturity to estimate the actual age of a person. It is usually performed manually by comparing an X-ray image of a left hand-wrist with an atlas, which contains a collection of images of known persons in the clinical procedure. The manual methods are based on analyzing special regions of the images of the hand bones or the whole bones of the images. Both approaches are prone to observation variability, time-consuming, and decision made on bone age is subjective. As a result, there is a pressing need to develop an automated method for bone age assessment. This research aims to develop an automated system for bone age assessment using images of the hand and the clavicle. Our research uses a new image processing technique that involves generating the histogram of the X-ray images. This approach overcomes the image segmentation problem, and it also overcome problems when conducting BAA on people who have hand defects or even growth abnormalities in hand bone. The technique can also overcome the problem of handling noisy hand images by using the clavicle images. A questionnaire survey and interviews were conducted in the Faculty of Medicine in University of Malaya Medical Centre (UMMC), to get an overview of the implementation of BAA at UMMC and to gather the users’ requirements for the development of an automated BAA system. The system was developed based on the Analysis, Design, Development, Implementation and Evaluation (ADDIE) model. The automated system called BAASHC (bone age assessment system using hand and clavicle) was evaluated on its performance and user acceptance using the SUMI-based questionnaire. The results of evaluation show that our system is a reliable and highly accurate solution for bone age assessment. Overall, BAASHC is not only useful to radiologists and doctors in the daily clinical practice, but it can also be used in forensic investigations.

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Dedication

This thesis is dedicated to my devoted parents, who introduced me to the joy of reading from birth and for their endless love, support and encouragement.

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List of Abbreviations

AAF	African-American Female
AAM	African- American Male
ADDIE	Analysis Design Development Implementation and Evaluation
ASF	Asian Female
ASM	Asian Male
BA	Bone Age
BAA	Bone Age Assessment
BAASHC	Bone Age Assessment System Using Hand and Clavicle
CA	Chronological Age
CAD	Computer-Aided Diagnosis
CAF	Caucasian Female
CAM	Caucasian Male
CASAS	Computer-assisted Skeletal Age Scores
ERD	Entity Relationship Diagram

FAE	Forensic Age Estimation
GP	Greulich and Pyle
GUI	graphical user interface
HIF	Hispanic Female
HIM	Hispanic Male
ISD	Instructional Systems Development
PACS	Picture Archiving and Communication System
PROI	Phalangeal Region of Interest
ROI	Region of Interest
SUMI	Software Usability Measurement Inventory
TW	Tanner and Whitehouse
UM	University of Malaya
UMMC	University of Malaya Medical Centre

Chapter 1: Introduction

1.1 Background

Bone age assessment (BAA) is one of the most important clinical procedures to determine the difference between the skeletal bone age and the chronological age (the real age from the birth date). This age discrepancy could indicate abnormalities in skeletal growth or/ and hormonal problems in children (Zhang et al., 2007). Recently, bone age assessment (BAA) has attracted much interest from the academic and medical communities. Bone age assessment, often expressed also as skeletal age assessment, is one of the most important issues in forensic science and medicine, as well as in physical anthropology, for the purpose of human identification and biological profiling on both the living and the deceased **(**Franklin, 2010**)**.

BAA is a skill in forensic science defined as Forensic Age Estimation (FAE) for the purpose of providing the most accurate value for the chronological age (CA) of an unknown subject in criminal investigations (Paewinsky et al., 2005). The expression of estimation is explained more clearly than other terms for diagnosis, and shows the main limitations in this skill. Forensic Age Estimation is not an introduction to a new field of skill in forensic science and judiciary history, as the eruption of the second molar was used in the Roman Empire as an indicator for calling young males for military service (Schmeling, 2008). In the nineteenth-century, age was estimated by dentists, and tooth eruption was considered to be a reliable method to detect the age of a child. In that era, the minimum criminal age was calculated to be 7 years old in Britain. However, some experts have objected to this method for the estimation of age. In 1846, Dr Pedro Mata expressed his concern about estimating age based only on tooth eruption (Bandelt et al., 2001).

Rontgen (1985) discovered X-rays in and his discovery triggered a revolution in the estimation of age for living subjects (Mould, 1995). This innovation, based on radiography of the skeleton, was used as a complement to tooth eruption in forensic practice. In 1886, Angerer was the first person who stated that the carpus bone in the hand is an indicator for the estimation of age in young people (Brothwell, 1981). The researchers tried to define the age of the subject based on the radiologically defined maturation of the human skeleton. Between 1950 and 1980, the most important methods for the estimation of age based on radiological analysis of the carpus bone were defined as Greulich and Pyle (GP), and Tanner and Whitehouse (TW) methods (Greulich & Pyle, 1959). There are many disadvantages concerning the accuracy of these traditional BAA methods. Firstly, the manual approaches in BAA are prone to the observer’s variability and this issue decreases the accuracy of bone age assessment at the stage of development. Secondly, bone age assessment using these methods are largely limited to subjective decisions, meaning that assessment using these methods is dependent on the experience of the radiologists or doctors who assess the bone. Thirdly, these manual approaches are very time-consuming (O'Keeffe, 2011).

In Europe, age assessment of living subjects was not needed until recently, as the counting and surveying of the population was precise and the reports could be used to verify the age of a citizen. European countries, however, have suddenly witnessed a huge influx of immigrants from other countries, especially in the last two decades, most of whom do not have any evidence to show their chronological age. This problem becomes even more complicated for immigrants who have the appearance of a minority. European legislation and courts of justice have to treat cases concerning minors in a special manner. It is not clear as to the number of young immigrants (minors) to European countries annually. In Germany and Spain, the legal framework of the Government faces a major problem in registering immigrants who are minors. In 2008, the Federal Office for Migration and Refugees of

Germany claimed the number of immigrants to be 763 persons and that 438 of them were between the age of 16 and 17 years, while the rest were below 15 years. In 2007 and 2008 most of the immigrants were from Iraq and Afghanistan, while between 2003 and 2006 most of the immigrants who were minors, were of Turkish, Russian, Nigerian, and Chinese origins. The census of minor immigrants in Spain revealed about 6,000 people with no known chronological age in 2008. Most of them were from Morocco and Sub-Saharan Africa who had arrived in trucks and dangerous boats via the Mediterranean Sea (PICUM, 2008). Most of these people in both Germany and Spain were male. Until now, there has been no standard method for the estimation of age among illegal immigrants in European countries. Some countries, such as the UK and France, hold an interview without any expert examination with people who does not have any identification papers. Since 2010, Austria has implemented the multifactorial method which consists of three levels: an evaluation by a doctor; a dental examination; and X-ray analysis, with low confidence. Hence, criminal proceedings and Public Courts in the Migration Network of European countries need an accurate and effective forensic method to address the problem of unaccompanied minors and provide an age estimation report (Schmeling et al., 2011).

This study was conducted with the aim of developing a new automated method for bone age assessment (BAA) based on the X-ray images of the hand and the clavicle for the living people. The methodology, design and implementation of the system will be discussed in the relevant chapters. It is hoped that the system could be used for age estimation by law enforcement agencies as well as in medical institutions for legal and forensic purpose.

1.2 Applications of bone age assessment (BAA)

Bone age assessment has four main applications:

1.2.1 Diagnosis of growth disorders

Growth disorders in children could be attributed to hormonal or non-hormonal reasons. The non-hormonal causes include genetic disorders, kidney diseases and malnutrition, while the hormonal causes include disorders of the sex or thyroid hormones and problems associated with diabetes. Most of these causes can be detected by blood tests in the clinics except growth hormone deficiency, which is more difficult to detect. Growth hormone deficiency can affect skeletal development and certain metabolic functions, and hence, it is crucial to detect such a deficiency (Clark et al., 2011).

Generally, the examination of growth disorders in children includes measurement of height, weight, growth rate as well as a clinical assessment of bone age. Kalpan (1982) stated that when a child has an inherent defect in skeletal maturation it is manifested as slow bone growth and delayed bone age. In fact, bone age assessment can be an indicator of the disharmony between bone growth and skeletal maturation. Although bone age assessment plays a crucial role in the detection of growth disorders, it is not clear how it can be used to estimate the bone age accurately. The Growth Hormone Research Institute suggested that any estimation of bone age in children should be done by an expert person but does not mention anything about the mean error that is acceptable or the desired degree of accuracy, and what is meant by an expert person.

1.2.2 Estimation of height

Marshall (1997) predicted children's height from the psychosocial perspective of both children and their parents. The methods for the estimation of bone age have been used with the method of predicting children's height. For example, Roemmich et al., (1997) studied 23 samples and used three approaches that based on three ways of assessing bone age, for the estimation of height. They were aware that an important reason for error in the estimation is the bone age, and that it is more visible at the age of puberty. Also, they found that part of the error in BAA was related to the population that was used as reference. Buckler (1983) claimed that in the estimation of height the errors that occurred are associated with errors in bone age assessment.

1.2.3 Control of treatment using growth hormone

Certain types of growth disorders due to growth hormone deficiencies are treatable by synthetic growth hormone. The treatment is very expensive, and moreover, many countries have special rules to monitor and control the use of synthetic growth hormones. In 2002, the National Institute for Clinical Excellence estimated that the price for treating a child of 30 kg with growth hormone deficiency was around £ 6103 in the UK, while in Australia it would cost approximately A$ 16 million dollars a year for children under the age of 20 years (Werther, 1996). The high cost is the main reason for the recent interest in finding a method of treatment that would optimize costs.

The policy also considers the selection of children who are more appropriate to receive treatment in order to control the children's reaction to the treatment, to give more hormones if it is really necessary and to understand the time for stopping the treatment. Different nations have various criteria and rules pertaining to bone age assessment in treatment optimization. Bone age is used by physicians to decide on the time for starting and stopping the treatment. The steps in bone maturity are considered to monitor the actions of the growth hormone. For example, the programme of the Department of Health and Ageing Australia for controlling the use of growth hormone recommends bone age assessment once a year, and to continue treatment, the patient must show 50% growth speed in bone age, otherwise the dose of the hormone will be increased after six months (Thelen et al., 1998).

1.2.4 Forensic science

As mentioned earlier, bone age estimation is one of the important procedures in forensic practice. It has been merged with forensic science to provide an expert's determination of age that can be presented in the criminal courts when there is no evidence to show the birth date of the child. Usually, it is used to identify unknown people who have died in suspicious circumstances or in mass fatalities (Warren et al., 2000).

1.3 Statement of the problem

In view of the large number of cases that require investigation of bone age, there is a pressing need to introduce an automated system for bone age assessment. In 1989, the first semi-automated system for bone age assessment (BAA) was developed based on segmentation of bones in a hand X-ray radiograph (Michael & Nelson, 1988). Automating the age assessment procedure in medicine speeds up the process of human identification, and thereby saves money.

Although, the numbers of automated systems for BAA have increased, most are still within the experimental phase because they do not produce accurate results (Rosenbloom, 2012). Moreover, there is presently no robust computerized method for bone age assessment in the health environment, partly due to the limitation in image analysis and image processing techniques, (Pietkaet al., 2001).

As a result of the rapid development in digital technology, a number of automated approaches for BAA have been developed, in particular, systems that process and analyze digital images segmentation of the hand. These systems estimate bone age by extracting and analyzing images of normal regions of the hand. These systems do not process images of abnormalities of the hand caused by trauma or those that are congenital in nature or those from unexpected trauma in forensic cases (Goldberg et al., 2012; Fischer et al., 2012). Another concern of this study is the inability to conduct bone age assessment for people who have pathological problem in their hands or even very noisy hand images.

The work undertaken in this research will result in the development of a new automated BAA approach that is based on analysis of X-ray images for the hand and the clavicle bones.

1.4 Objectives

This research aims to develop a web-based system for assessing bone age by using X-ray images of bones to improve computational forensic science. The specific research objectives include:

1) To identify the factors that can affect assessment of bone age.
2) To design and develop an automated system for bone age assessment based on the X-ray images of the hand and clavicle bones.
3) To evaluate the accuracy and usability of the proposed bone age assessment system.

1.5 Research questions

Bearing in mind the aims and specific research objectives, the development of the BAA system is also aimed to answer the following four research questions:

1. What variability should be considered in the development of a computerized system for bone age assessment?
2. What are the factors that can contribute positively to automated assessment of bone age in the clinical environment?

3. What methods can be applied to implement a system to overcome the limitations of the existing systems?

4. How will an automated system for BAA benefit the radiologists and forensic experts?

1.6 Research methodology

This research uses both quantitative and qualitative methods to collect data. The methodology used involves the following steps:

i. Conducting a literature review to get a comprehensive view of the research topic and to identify the factors which are pertinent to the design of a BAA system based on the most suitable technology.

ii. Conducting a questionnaire survey to understand the main issues concerning BAA based on the feedback from the radiologists in UMMC.

iii. Conducting a structured interview with the medical specialists to get a more detailed understanding of the key issues pertaining bone age assessment and the current challenges faced in the research in this topic.

iv. Conducting observations to fully understand the methods that radiologists use to assess bone age in the University of Malaya Medical Centre (UMMC).

v. Designing a new BAA system based on the use of X-ray images of the hand and clavicle.

vi. Evaluating the accuracy of the developed system.

Detailed information was collected from those who are experienced in the bone age assessment process. The data collected in this research will be divided into four levels as shown in Figure 1.1.

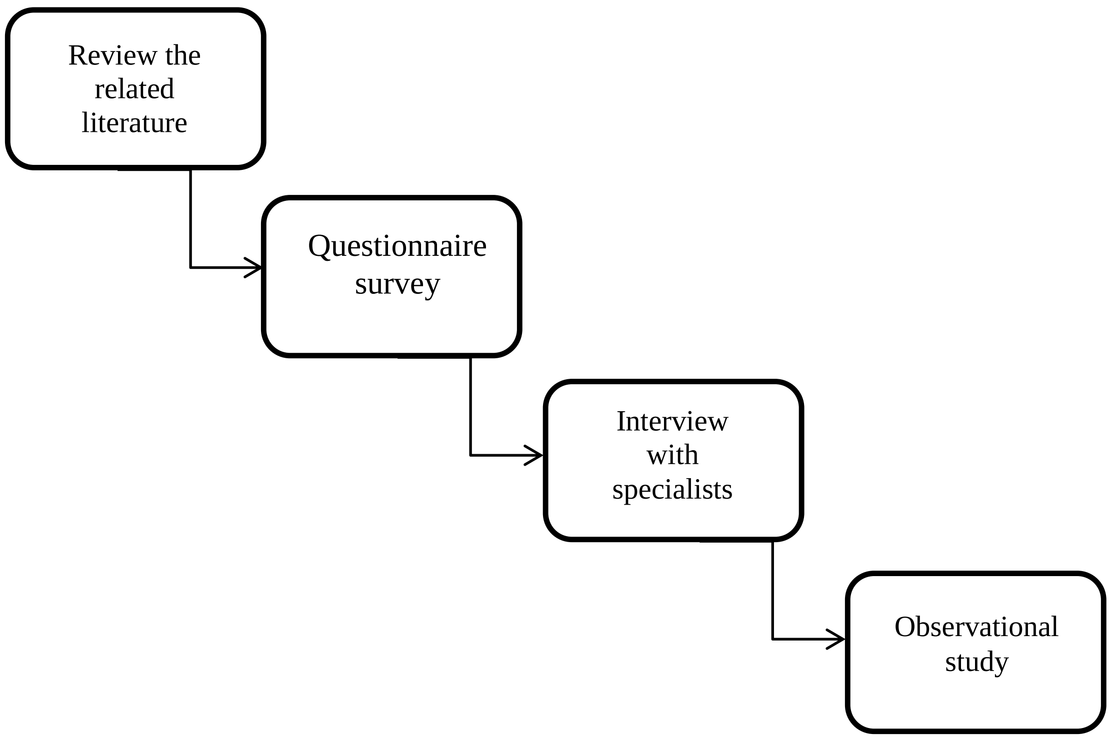

Figure 1.1: The process of data collection

Level 1 involves compilation of the knowledge on BAA gathered through the literature review. The information gathered will also give a clear direction to the research. Specifically, the information gathered includes:

- History of bone age assessment procedures
- A taxonomy of different methods in BAA from manual approaches to the automated approaches
- Identifying the problems encountered in BAA.

Level 2 involves a questionnaire survey to investigate the BAA practices in UMMC. The goal of the survey is to identify the current situation of the BAA process in UMMC, the reasons for conducting BAA, the main challenges faced, and whether there is a need for an automated method for BAA to be implemented.

In Level 3, a structured interview will be conducted with the medical specialists at the Faculty of Medicine. The interview questions will be based on the questions (Berst et al. (2001)) used in their study on the critical factors that affect bone age, limitations in assessment of skeletal age, and motivational factors for implementing an automated system for bone age assessment.

Level 4 involves making observations (Refer Chapter Three) to find the BAA methods used by radiologists at the University of Malaya Medical Centre (UMMC). Observational study was carried out in the X-ray lab in Biomedical Imaging Department at UMMC. Extensive information was gathered from a radiologist on the application, significance and the challenges encountered in bone age assessment procedures and practices in UMMC.

1.7 Significance of the study

BAA has been a subject of great academic interest for a long time. The procedure is regularly carried out on children and juvenile for evaluating growth, management of limb length discrepancies, management of scoliosis, and the diagnosis of endocrine disorders and genetic disorders. The traditional methods that had been used to determine age are often not accurate. Hence, there is a growing demand for automated methods for determining an individual age with more accurate results (Mansourvar et al., 2013).

It is expected that an automated system would improve the accuracy of bone age assessment in both clinical practices and in medical research. The use of an automated system would decrease the costs of estimation bone age as a result of the time saved and the less manpower needed.

The manual methods have drawbacks because observations can be subjective. An automated system, on the other hand, would eliminate the observer's variability and also benefit from the intervention by experts to be more effective and accurate in the assessment of bone age.

1.8 Thesis organization

This thesis consists of seven chapters as follows:

Chapter 1 contains an introduction to the basic concept of bone age assessment and highlights the study problems and their significance. It also outlines the objectives of the research, the methodology and the research questions.

Chapter 2 discusses the review of published literature related to bone age assessment, the various methods used and their limitations.

Chapter 3 presents the methodology of the research, methods for data collection to identify the user requirements needed to develop the proposed system. This chapter also presents the framework of the proposed BAA system.

Chapter 4 focuses on the data collected from the questionnaire survey and analysis of the feedback from the interview with the medical specialists in UMMC.

Chapter 5 discusses the design, and implementation of the system as well as the methods and concepts used in the system development. It also discusses the programming language used and the database of the proposed system.

Chapter 6 involves evaluation and testing the performance and the usability of BAA system.

Chapter 7 discusses the research findings and conclusions. It also includes recommendations for future researches.

1.9 Conclusion

In summary, this chapter presented the introduction of the research, an overview of bone age assessment (BAA) and its application, the motivation for developing an automated system for BAA, and the challenges faced in research on the topic. The research objectives and research questions were also presented in this chapter.

The next chapter reviews the studies that have been conducted on BAA and highlighted the problems encountered in these studies.

Chapter 2: Literature Review

2.1 Introduction

This chapter presents the theoretical and historical reviews of previous researches carried out on bone age assessment (BAA). It discusses the existing BAA systems and how they have been implemented. This chapter discusses mainly two aspects of BAA gathered from the literature reviews. The first aspect pertains to the research on BAA systems based on hand X-ray images. The strengths and weaknesses of the features in all the systems are described. This is followed by a discussion on the role of the clavicle bone in bone age assessment. The second section of the chapter discusses the improvement that can be made to the automated BAA system by using the clavicle bone of children with pathological problems or growth abnormality of their hands.

2.2 The need for age assessment

In 2010, UNICEF stated that only about 50% of children below five years of age in the developing countries have birth registration documents. For example, 64% of births in sub-Saharan Africa and 65% of births in South Asia are unregistered. This unregistered are deprived from the rights they deserved. Without any evidence to indicate their age, children are at risk of underage recruitment into the fighting forces, and forced into early marriage. They are more vulnerable to judgment as an adult rather than as a child or juvenile in criminal courts or when seeking for international protection as an asylum seeker (Smith & Brownlees, 2011).

Children without any identification ID or birth document, have less chance for leniency in sentencing in courts or the benefit to be put into the facilities in juvenile rehabilitation centres, and are also treated as adults for issuing penalties in law enforcement. When a juvenile is wrongly identified as an adult it could change his/her life in consideration of the maturity, capacity or ability in reintegrate. To be considered as an adult places a child at risk of a cycle that is disproportionate to the situation, age or maturity. Children deserve special protection and are below the age of criminal responsibility, and some may enter the formal justice process through incorrect identification. Hence, a realistic definition of age is crucial to decide and treat children and juveniles properly. Unregistered migrant children are at great risk of abuse and discrimination.

Unregistered or migrant children are vulnerable to many kinds of prejudice and injury. In 2007, some unregistered refugee children in Guinea were arrested arbitrarily by police and other law enforcement as adults, and they were unable to assert their age. Refugee children in Europe had been in a similar position (Ruxton, 2003). They have been entered into the adult asylum determination process because their age was not clear. They were deprived of any concessions that are of benefit to children. In the UK, this position means that they have more limited rights for the asylum interview, do not benefit from having a lawyer to support them at the interview, and are even detained during the decision-making process (Crawley, 2007). Being considered as an adult provides the refugees with special facilities and financial assistance. Positive decisions have been made through national campaigns to register the birth date of children refugees. Afghanistan and Bangladesh have created their first government birth registration systems, while India and Pakistan have tried to promote birth registration in Asia (Cipriani, 2005).

Despite this development and the attempts by UNICEF and other international organizations, many children still do not have registration documents. Hence, when a government or any agency wants to estimate the age of an unregistered child they need a secure and accurate method of assessing the age.

In the rest of this chapter, the literature on the various methods for bone age assessment and the factors that could have effect on the age estimation process are reviewed. It will discuss the different methods that have been applied and will be compared.

2.3 Methods of age assessment in the living

In the year 2000, with the increase in cross-border migration into European countries, the Study Group in Forensic Age Diagnostics (AGFAG) was established in Berlin. This group, which included many professionals from Europe, was established to examine age estimation methods, the accuracy and the reliability of the methods based on modern day requirements. The group had collected a huge volume of data and their research had led to set of information to allow it to make reasonable estimate of the age of human that is enough to qualify for submission to a court. The various methods identified are based on four criteria (Schmeling *et al.*, 2008):

- Physical health;
- External physical characteristics;
- Skeletal maturity; and
- Dental maturity.

Most of the European countries applied radiographic imaging to estimate the age and the remaining few countries used other methods. The situation in the UK is totally different where age estimation is based on psychosocial factors rather than biological factors or radiographic imaging in the majority of cases (Baldwin, 1997).

Skeletal maturity is based on the examination of radiographs of the left hand-wrist. If the subject is older than 18 years, the method can be used together with the images of the medial clavicles to reduce uncertainty of the result (Singh et al., 2010).

Dental maturity, defined as dental age, is an indicator of growing children in biological maturity. Dental maturity is based on examination of an orthopantomogram using visualisation of the full dental arch (Liversidge et al., 2003). In the process of age estimation, the skeletal and dental images are compared to sets of source images as standards. The standard images are taken from various sections of the populations and of different sex and age. Most of the methods used dentition estimated age based on eruption and completion of the roots of the second molars (Frisch et al., 1996).

2.3.1 Assessment of skeletal maturity

The assessment of skeletal maturity is a clinical procedure and is often referred to as bone age (or Bone Ageing). It is usually based on the imaging of two body parts:

- The left hand-wrist; and
- The medial end of the clavicle.

An X-ray image of the left hand-wrist is commonly used for bone age assessment for the following reasons (Scheuer & Black, 2000):

a. This area can be separated from the other parts of the body, thus exposure to harmful ionizing radiation of the rest of the body can be minimized;
b. This hand- wrist area of the body includes a lot of ossification centres that appear or change morphologically or even fuse in the settled model;
c. The epiphysis of the distal radius is the last area to fuse, and occurs relatively late in adulthood (at age 16 to 20 years for males, and 14 to 17 years for females);

The above reasons justify why the hand-wrist area of the body can be used to estimate the chronological age during the period of childhood, for age assessment of a person who is in his/her late teens to early 20s or if the bone development of the hand has been completed, a CT scan of the medial end of the clavicle is suggested, also. Radiography of the medial clavicles is difficult because of overlying structures, hence, a CT scan is used for better visualization.

Age evolution from skeletal maturity is affected by different factors, such as ethnicity, sex, lifestyle, medication, nutritional status, drug addiction or medical disorders (Schmeling et al., 2005; Schmeling et al., 2006).

2.3.2 Factors affecting age assessment

Lucina (2012) categorised the factors that affect skeletal maturity in two groups:

- Inherent factors: as in genetic inheritance, sex, and ethnicity ; and
- External factors: as environment, nutrition, and health.

Over time, these factors have affected different population groups and also not in isolation- known as a secular change. Johnston (2000) explained secular change to be changes that occur during the time and in different groups of children in various stages of growth. This is why it is difficult to find any relationship between the chronological age and biological growth.

2.4 Age assessment from radiographs

Bone age assessment based on skeletal maturity is based on three aspects of bone growth:

- Appearance of primary and secondary centres of ossification;
- Growth of both the primary and secondary centres of ossification; and
- Timing of fusion of the primary and secondary centres.

The appearances and changes in the above processes have been clearly observed in dry bone and radiographic images (Flecker, 1932). Judgment about the age will no doubt be based on the identification of the time of appearance of the ossification centres, identification of epiphyseal fusion, and dependent on whether the dry bone is observed or it is being visualized by an imaging method like radiography (Coqueugniot & Weaver, 2007). The assessment of chronological age is based on a matching process that includes a comparison of a radiographic image of a subject with a defined reference which involves sample of known sex and age. The process of age estimation is basically a measure of the biological maturity that is converted to the chronological age by comparing an image with a defined reference (Black et al., 2011).

Reference data for age estimation have been collected from various sources and have been presented as a series called “Atlas“. Much of the data in the atlas had been collected during longitudinal studies that were carried out in the 1900s. The data were collected from each child as part of an anthropometric exercise in standardized radiograph format. Since the goal was to show the growth in normal life of all participants whose health histories, indicate absence of any disorder or disease. These data provide the reference data for estimating the age of unknown child for identification or medical or educational purposes. Generally, the atlases were developed for two main goals:

- To identify the individual whose growth is not normal, and to allow doctors to detect the degree of skeletal maturity;
- To investigate the health status of a population by measuring their growth and comparing the data with the atlas of known healthy children.

Factors such as environment and especially, nutritional status, can have a strong effect on the developmental growth of children in a society (Fernandez et al., 2007). The atlases on healthy children who had adequate nutritional intake would be suitable for use as the standard for comparison (Todd, 1930). These atlases included dataset of images which show the maturational changes as a powerful source for age estimation in the living. The atlases take the maturation steps of a child of unknown age and find the most proper age rather than evaluating the maturational steps of child with known age. This is a common use of most of the atlases, and the experts have designed a number of their methodological based on it.

The methodological issues are based on two principles:

- The methods have been developed in way for which they were never intended. Rosenbloom and Tanner (1998) suggested a "wholly illegitimate use" that must be avoided, or is it possible to apply the technical methods and present them as robust methods to the court?
- The atlases present a temporary snapshot of the maturational tempo of children of a known race. The problem is whether this information is related to a modern society or can the atlas be used for children of different races with different diet and different access to medical care.

The danger of exposure to X-ray is another challenge that researchers should consider during data collection. It is also legally wrong as well as ethically not right to collect radiographic data without prior permission (DEFRA, 2004).

Designing and developing of age assessment methods based on bone images are still in their infancy. Hence, the forensic experts are not able to collect data on the same scale or as detailed as the studies done in the 1900s. Currently the forensic researcher is only able to review the atlases that are available and to treat them as the relevant, valid and robust information for reference.

Many of the publications on BAA had suggested that the atlas used for age estimation should be based on the left hand-wrist bones. The type of researches conducted can be classified based on the methods used to test accuracy include (Yasemin et al., (2003); Cameriere et al., (2006); Schmeling et al., (2006); Gilsanz & Ratib (2005)) :

- Testing age estimation methods on special society;
- Comparing the errors observed;

- Comparing the accuracy of different atlases from the same skeletal area on the same group;
- Comparing the maturity levels of the different body parts, on the same group.

2.4.1 Choice of the left hand-wrist for skeletal maturity assessment

Assessment of skeletal age is possible using many bones in the body. However, the high costs, long interoperation, and the risk of exposure to radiation show that this is neither suitable nor practical for most of the body parts (Kaplan, 1982). The researcher investigated the overall development of the skeleton and explored various methods used for different body regions. The methods developed are usually based on one part of the body out of 100 possible centres of ossification (Graham, 1972). The regions considered include the foot, shoulder, ankle, hip, elbow, cervical spine, and the hand-wrist (Leiteetal, 1987).

For a skeletal age estimation method to be useful, it must be applicable for various types of skeletal development. Some skeletal age estimation methods have limited application because of the limited region of the body they are used for. For example, the Sauvegrain system which works with the elbow, is not so useful because it only works at a particular stage of growth when the elbow shows radiographic changes from 10 to 13 years for girls, and from 12 to 15 years for boys (Dimeglio et al., 2005).

One of the areas of the skeleton, which has been identified as the most effective for age assessment, is the left hand and wrist. There are some bones in the hand and wrist whose change sequences parallel the changes of physical maturation (Tanner et al., 2001).

Generally, most people are right-handed so the left hand has less chance to be modified or hurt in unexpected events, which is the reason that researches prefer the left hand for the assessment of bone age. However, although some researchers used the radiograph of both the left and right hands, the results show that there was no significant difference whether the image of either hand is used (Roche et al., 1988).

2.5 Manual methods in bone age assessment

As mentioned above, bone age is defined as an indicator of skeletal maturity from the radiography of the ossification centres. Despite the large number of scientific researches on bone age assessment, there is a lack of agreement concerning the accuracy of bone age assessment methods which can be accepted for use in the clinical environment.

The three main manual methods of bone age assessment based on the use of the hand-wrist radiographs include: the Greulich and Pyle (GP) method (Greulich & Pyle, 1959); the Tanner and Whitehouse (TW) method (Tanner & Whitehouse, 1996); and the Fels method. The TW method and Fels methods are scoring methods, while the GP method is an atlas-based method. Section 2.5.4 provides a critical comparison of the three methods. To have an in-depth understanding of the terms used BAA, it is necessary to understand the anatomy of the hand.

Bone age assessment (or assessment of skeletal maturity) involves the analysis of different centres of ossifications such as:

- carpal bones;
- epiphyses (includes: distal, middle, and proximal phalanges);
- radius; and
- ulna.

The bones of the epiphyses ossify a few days after birth and increase over time in all dimensions. The epiphysis will extend until the edges of the metaphyses are reached. In adolescence, when the growth is complete, there is no gap between the epiphysis and metaphysis.

Carpal bones can also be used for estimating age in children. They are like small pin points in the early stages of growth and increase in size and shape in adults. The growth in girls is faster than boys of various ages. Johnston and Jahina (1965) stated that bone age assessment based on analysis of the carpal bones for children older than 9 or 12 years, is not a robust method because of the overlapping of the carpal bones at this age and that phalangeal analysis gives more valuable results.. Figure 2.1 shows a radiograph of the hand-wrist.

Figure 2.1: Hand wrist radiograph

2.5.1 The Greulich and Pyle method

Greulich and Pyle (1959) defined their method (GP) as an atlas-based method. In this method, bone age assessment is conducted by comparing a radiograph of an unknown child's hand with a reference in the atlas, which includes radiographs for different age ranges. The atlas is checked for standard refrence that provides the closest match to the unknown radiograph. The GP method uses the chronological age to assess the skeletal age, and then compares the unknown image with the atlas before and after chronological age assessment (Mansourvar et al., 2013). A preliminary selection is done by comparing the X-ray image of the unknown subject with the standard images and determining the maturity stage of skeletal development, such as epiphyseal fusion. The GP method needs an expert to work simultaneously through the selection of radiographs, and compare each of the 31 bones in the hand-wrist with the images in the atlas. The age of the bone is estimated by using information in the standard images, including the closest size to the image. Figure 2.2 shows the procedure for bone age assessment using the GP method.

The atlas includes outline drawings and information about indicators of skeletal maturity to help the expert in matching the level of maturity. In addition, each radiograph includes some explanatory notes on the basic indicators of skeletal maturity in relation to the skeletal age. If each bone in the image of the unknown subject could be matched to a single standard in the atlas, the new case would be assessed. If the exact match is not found and the match is between two standard radiographs, then an average of the two standard images is considered as the estimated age. Greulich and Pyle did not provide any suggestions concerning how to do the calculation, but Roemmich (1997) used the median of the ages of the bone to implement the GP method. The atlas includes 27 standard images for females, and 31 standard images for males. The images start with 3-month intervals and continue to 6-month intervals at 1.5 years, then decrease to annual intervals from ages 5 to 18 in the section for females, and 19 years in the section for males. There is an extra standard at 13.5 years for females, and 15.5 years for males, because of the rapid speed of skeletal changes during the age of puberty. The lack of sufficient standard images at the time of puberty reduces the accuracy of the age estimation and increases inter-observer error. This problem has been highlighted as the main disadvantage of the GP method (Zhang et al., 2007).

The GP atlas contains the standard images of one hundred children of the same age and sex. The images were chosen based on the relative skeletal status or as an indicator of the central tendency or anatomical mode (Greulich & Pyle, 1959). Professor Wingate Todd, during his research in Western Reserve University of Medicine in Ohio, between 1931 and 1942, collected one hundred images for each standard images from 1,000 radiographs of known children.

Researchers believe that children with a high class level of nutrition and education mature faster, hence the radiographs included in the atlas of this level have been deemed as too advanced for the actual age. This issue is an important criticism of the GP method (Cox, 1996; Tanner & Healy, 2001).

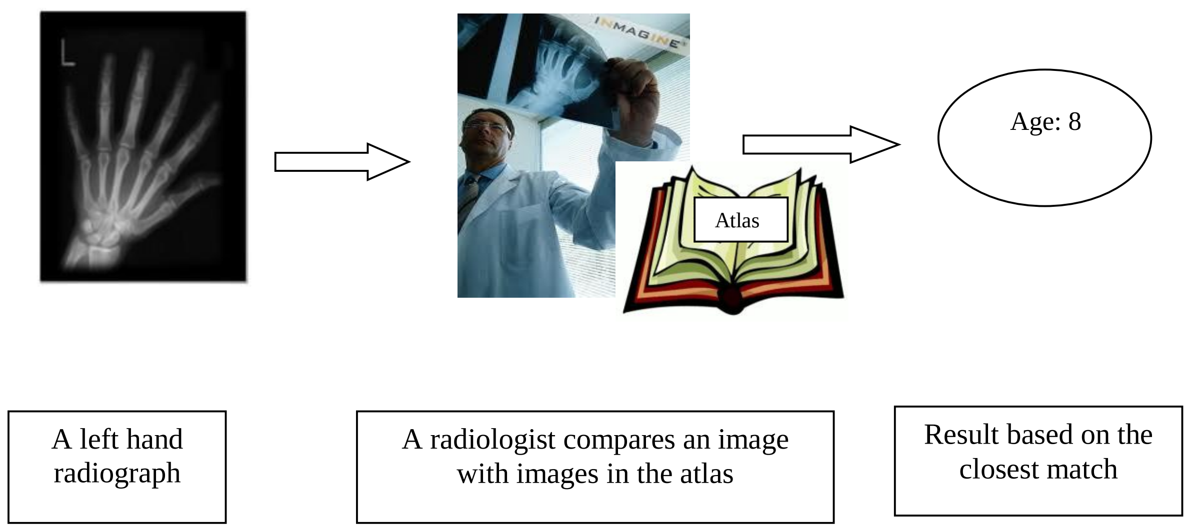

Figure 2.2: Procedure of bone age assessment using the GP method

2.5.2 Tanner and Whitehouse method (TW)

Tanner introduced the Tanner and Whitehouse method (TW) as a score-based method in the 1960s. This method includes independent staging of up to 20 bones of the hand. Each bone is divided into eight to nine separate stages that cover from the beginning of ossification to the full level of maturity in the bone. The stage is selected by trial and error, hence, the movement between one stage to another stage is not too large to lose data or too small to confuse or increase the error rating (Tanner et al., 2001).

Each stage is assigned a letter from A to I, as shown in Figure 2.3, and each letter reflects the level of bone development.For example, A means that no sign of the bone is observed:

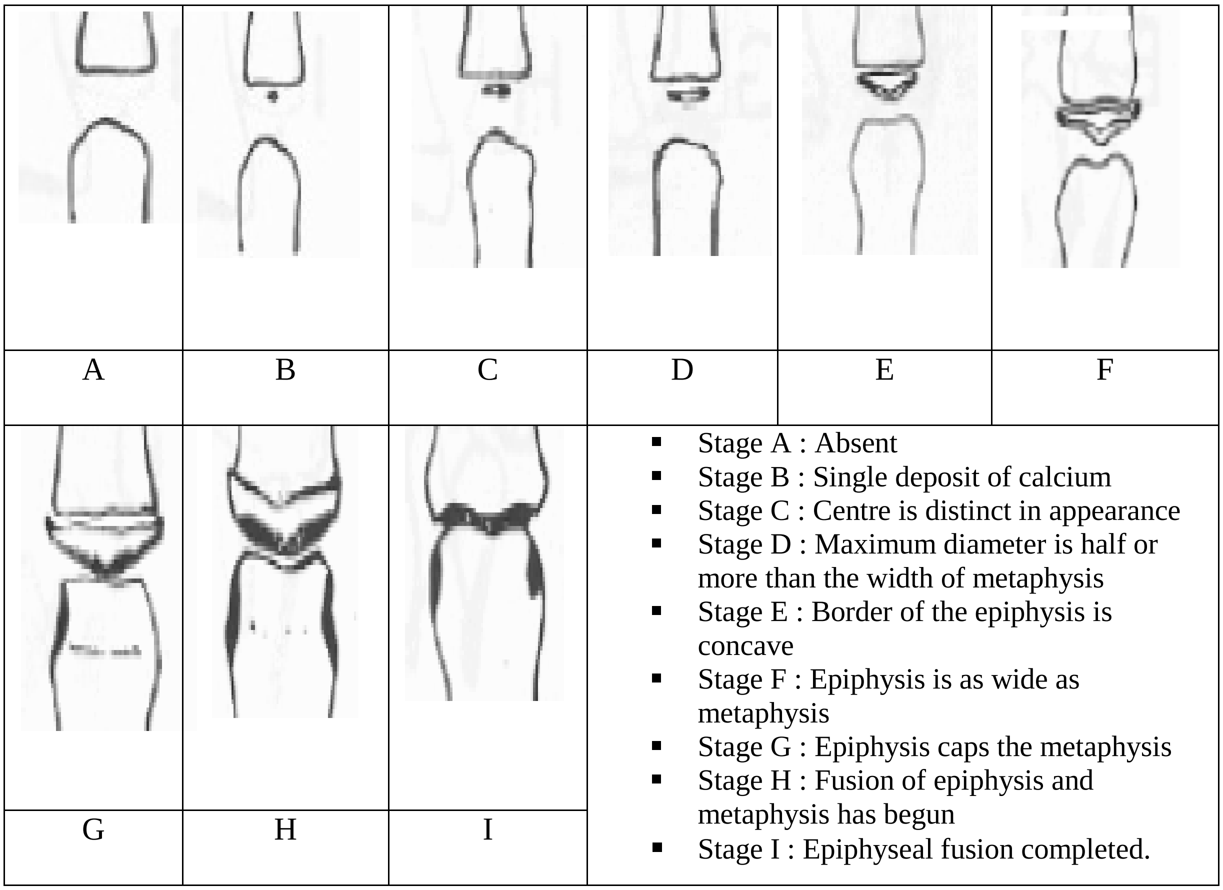

Figure 2.3: Stages of phalanx bone growth in TW method

Each stage includes up to three criteria and a diagram of the usual features. Some criteria define the distance between bones or the ratio of the size of bones. Hence, it is essential to specify the distances. This method does not use the overall standard radiographs, but only cropped X-ray images, which are typical for the bone stage being assessed. The stages and also the criteria are independent of the sex, ethnicity and social state of the patients (Cox, 1996).

The relationship between each stage and a maturity score shows the overall difference among the bones of an individual. The scores are determined based on analysis of a huge sample of bones in different ranges of age from early childhood to adolescence. The scores are classified and the sum of the scores indicates the degree of development, for example 0 represents invisible status and 1000 represents full maturity status. To determine the skeletal maturity using the TW method, it is necessary to assess the stages of bone growth, the score for each stage and then sum all the scores. The skeletal maturity score represents the bone maturity, which in the TW method, is independent of ethnicity, social conditions or education. The TW method uses some scales of maturity that are independent of age, such as height and weight. However, many researchers prefer the use of bone age to measure maturity. The chronological age is assessed based on bone age, which is obtained from the skeletal maturity scores. The TW method uses a sample of 2,700 healthy children from Scotland and England between 1950 and 1960. The first version of this method includes the various growth stages of 20 bones: 13 long bones (radius, ulna, metacarpals, proximal phalanx, middle phalanx, distal phalanx) and seven carpal bones (capitate, hamate, triquetral, lunate, scaphoid, trapezium, and trapezoid). The revised version of the TW method was defined by the TW2 method between 1975 and 1983 (Tanner et al., 1983).

The TW2 method uses three scores based on different parts of the bones. This method also considers 20 bones: 13 bones of the RUS (Radius, Ulna and Short bone score: finger bones) and seven carpal bone scores. The TW2 method separates the RUS and carpal bone scores based on their different status of maturity (Tanner et al., 1983). In the TW2 with carpal scoring method each carpal bone assumes an equal weight against the others, while in the

TW2 with RUS-based scoring, the radius and ulna assume higher weight compared to the metacarpals and phalanx of the same maturity status. The weights for the scores are considered for each stage and the sum of the scores is applied for assessing the bone age. The third version of the TW method is TW3, which was released in 2001. The TW3 method only uses the RUS and carpal scores for the maturation stage. The TW3 method presents a new reference group for the TW2 RUS scores while using the same carpal scoring system (Tanner et al., 2001).

2.5.3 The Fels method

Roch et al. (1998) defined the Fels method as a score-based method that uses 98 skeletal maturity indicators and 13 measurements. The indicators and measurements include a series of processes – publishing the description to clarify, reviewing, grading, and testing. About 25% of the indicators in the Fels method are used for assessing the age of a new case. The data are saved in a table and any new case is checked as to which indicators should be assumed. This method uses 22 bones for age estimation: 20 bones are the same as in the TW2 method with the adductor sesamoid and the pisiform bones. The indicators of maturity for the bones were evaluated based on a written description, line drawings and sample radiographs. The indicators could be in two grades or more than two grades, for example: the beginning of ossification, the bone shape or the ratio of the epiphyses.

When the bone of the sample has been graded using the indicator, the grades are processed using a computer program and the bone age is estimated with the error rate. The software uses a model based on probability, which is adjusted for the indicators. The bone age is estimated as a maximum estimate of the trace line to get the observed information.

The samples for the reference in the Fels method were collected from 667 children from south-western Ohio, and from different cities, small towns and villages, and from people of various socioeconomic status. A total of 13,823 images were gathered between 1932 and 1977, which covered the span of maturity from 1 month to 22 years.

Although it might appear that the TW and Fels methods have a similar function, they have major differences. The basic difference is that the TW method is used for estimation of age but does not use chronological age, while information on the chronological age is needed in the Fels method. The next difference relates to the scoring. The Fels method grades the maturity indicators and is based on multiple grades for bone age assessment whereas the TW method is based on maturity indicators to assume a stage for each bone. The third difference is that relative measurements are used as maturity indicators in the TW method and as continuous maturity indicators in the Fels method.

2.5.4 Compression between the manual methods

The main problem in testing the accuracy of bone age assessment systems is that there is no unique gold standard. One method selects a group of normal and healthy children and compares their chronological age with the estimated bone age. This method is similar to a cross-sectional evaluation. Comparative research however, not only compares the estimated age of one method with the chronological age, but also compares different methods for bone age assessment with each other.

The accuracy of each method has a direct relationship with the population that is used for reference, and also the population that uses it for measurement. Evaluation is done by applying the assessment techniques. For example, if the user has not received sufficient training, then the probability of error will increase in the matching process.

The main problem in all manual methods (e.g: the GP method) is that they are subjective in assessing the skeletal maturity. The TW and Fels methods are more credible because they use systematic techniques for assessing (Roche et al., 1988).

Hence, the different results obtained when comparing the three methods are due to the different references, subjectivity of evaluation, and selection of the skeletal maturity for testing. For example, one research compares the three methods by choosing 23 boys at the age of puberty. The test results show that for a sample population with age ranging from 9 to 15 years, the TW2 method is more advanced than the Fels and GP methods. In general, the Fels results are more accurate than the GP method for the younger children, while in teenagers, the Fels method is less accurate than the GP result for the male and female samples. When comparing the Fels and TW2 methods, the revers results are obtained. For a sample ranging in age from six to nine years, the TW2 method is more than two years larger than the Fels method for females and 1.7 years more for males: for the younger population sample, the two methods produce the same results, and the differences between the TW2 and the Fels methods, is smaller for the children at the age of puberty.

The big difference between the TW2 method and the Fels method is the different populations used for reference. The other basic difference between the three methods is the variability in the maturity of the bones, except for the reference population. This difference has more effect on the GP method than the TW and Fels methods, roughly. This problem can be solved by isolating and summing the scores to assess the bone age.

There is no agreement among the researchers as to which of the three methods produces the best result for bone age assessment. Albanese et al. (1995) suggested that each method could be more useful in a particular situation. Buckler (1983) conducted a survey among 182 pediatricians from Wales and England, and the findings show that 76% of them prefer the GP method for bone age assessment, while 20% prefer the TW method, and 4% prefer the other methods.

Zerin and Hernandez (1991) stated that the GP method is the favourite method in the United States while Greenspan and Gardner (2001) identified the TW method as the most widely used in Europe. In 1997, Marshal expressed that the TW2 method was too difficult for daily use while the GP method was adequate for reasonably accurate estimation. The GP method is the preferred method due to its ease of use and also the shorter time needed to make an assessment.

King (1994) estimated the time taken to conduct bone age assessment as 1.4 minutes using the GP method, and 7.9 minutes using the TW2 method. The maximum range of age which can be estimated is different for three methods_ 16.5 years for TW method, 18 years for the GP method, and 18 years for the Fels method. (Greulich & Pyle, 1959).

The three methods discussed previously categorized as manual approaches in BAA are presented in Table 2.1. Each method had been evaluated against reference criteria discussed in Section 2.4.

Table 2.1: Comparison of manual approaches in BAA

Approach	**GP method**	**TW method**	**Fels Method**
Basic Theory	Atlas-based method	Score-based method	Score-based method
Investigator	Greulich and Pyle	Tanner and Whitehouse	Roch and Thissen
Presentation Date	1959	1960	1998
Main advantages	Easy to use	More accurate result	More result credible
Main Problem	Subjective decision	Time-consuming	Time-consuming

Time of Estimation	1.4 Minutes	7.9 Minutes	7-9 Minutes
Popularity in Wales and England	76%	20%	4%
Popularity in US	Favourite method	--	--
Popularity in Europe	--	Favourite method	--

2.6 Automated approaches in bone age assessment

For assessment of bone age in both the clinical environments and the courts of low, it is important to yield the most accurate result. An automated bone age system could reasonably eliminate the role of a human observer, and this would decrease the subjectivity in assessment, which has been the main reason for inaccuracy in the assessment.

Most of the automated systems for estimation of bone age estimate skeletal maturity based on X-ray images of the left hand-wrist. This poses some difficulties because the hand-wrist area has various bones, which change in shape over time, and also some bones overlap with maturation. As mentioned previously, analysing bone age is a complicated process even for experts. Most computer-based methods use the TW approach because of the scoring method used for skeletal maturity and the separate stages. Special image processing techniques are needed to assess the radiograph of a hand. Noisy or missing images or poor contrast of some sections in the images pose difficulties for automated bone age assessment.

Researchers in BAA have expressed that there are benefits in automating the method for the estimation of bone age. These methods involve the use of the some intelligent techniques such as segmentation of the hand, while some are only used purely for research. It is estimated that computerized methods of BAA could decrease the cost of assessing the bone age through a saving of the time radiologists spent in manually estimating the bone age. Some of the automated methods for bone age assessment are discussed below.

2.6.1 HANDX system

The first semi-automated system for bone age assessment was introduced by Micheal and Nelson in 1989. The authors claimed that this system, called HANDX, is able to automatically segment X-ray images of bones of the hand-wrist using image processing techniques.

This system reduces the variability of the observer, and from the results produced, they were able detect abnormalities of skeletal growth in children. This computer vision system works in three stages: pre-processing, segmentation and measurement stage. In the first stage, the radiographs are normalized to be inputted into the next stage. The segmentation stage looks for the specific bones in the hand and also isolates the edges of the bone. In the final stage, the quantitative parameters are determined. This semi-automated system is not accurate when the hand image is fused, and moreover, the system has never been evaluated on its performance on a large scale.

2.6.2 PROI based-system

In 1991, Pietka and his research group developed a method based on PROI analysis. PROI is the region of the hand that includes the phalanges and epiphyses. For the estimation of bone age, the system first scans a horizontal line and the lower boundary of the PROI is detected before the soft tissue between the thumb and first finger.

In the next stage, the upper boundary containing a horizontal line at the edge of the third finger is scanned. When the upper, lower, left and right boundaries of the PROID have been detected, the segmentation stage starts. A gradient image is used for segmentation of the bones and the output threshold is based on empirical analysis to determine the bone edges. The density of the pixels at the end of the region is higher than the cantre section. In this method, the boundary between the third distal, middle and proximal phalanges is measured. This measurement uses the standards table prepared by the Garn group (1972), that shows the method to convert phalangeal length to skeletal age.

The system has been evaluated by analysing 50 digitised radiographs (CR) of patients and comparing the results with that of an observer (radiologist). The mean difference obtained from the evaluation was 0.02 mm with a measurement error of 0.08 mm.

2.6.3 The CASAS system

In 1994, Tanner and Gibbons proposed a computer-based skeletal age scoring system, CASAS, based on the TW2 RUS method. This semi-automated system digitized X-ray images using a light box and a monochrome video camera. Every bone is located by the digital camera using an overlay pattern. The computer assesses the bone age by matching and finding the best average based on fast Fourier transform. The method minimizes the root-mean-square error between the coefficients of the Fourier transform from the unknown bone and the Fourier transform of the available bone templates. The patterns are produced by averaging the Fourier transform coefficients using 10 images of the bone development stages. The system improves to five-root-mean square by using a Gaussian function. The images are only applied to develop a standard image of skeletal maturity for the TW method and not for developing the actual bone scoring style. In the system, the templates play a vital role, and thus, selecting the source for making the templates is very important. The CASAS system has been tested and evaluated using X-ray images of bones from children in normal and stable health condition. Some researchers have compared the CASAS method with the manual TW method and the results show that the CASAS estimation is more accurate than that of the manual TW method. Frishch et al. (1994) stated that it is generally agreed that the CASAS system is a suitable method for bone age assessment for children in a normal situation. The system is based on a very simple image processing process, and the processes can be repeated. The main weakness is that the method cannot be used for assessing bone with pathological problems because of the deformation of the bone. The assessment using the method, is not objective because of the large number of manual interventions.

2.6.4 Middle phalanx of the third finger based on an active shape model

Niemeijer (2000) developed an automated system based on the TW2 method that classifies the middle phalanx of the third finger using the active shape model. The model uses the mean object, description of modes of variation and a covariance matrix for statistical measure. In this method, the radiologist specifies the third phalanx and the computer segments the bone with the active shape model. The matching function is executed by the highest relationship between the pixel scale for RIO (region of interest) of the unknown bone and the pixel scale of the sample images. The system was 73% to 80% more accurate when compared to the assessment of an observer. The drawbacks of the system are twofold: firstly, the system only works for stages E to I in the TW method; and, secondly, the system only assesses the bones of those who are aged between 9 and 17 years.

2.6.5 Neural network system based on linear distance measures

Gross et al.(1995) developed a system by using a user to measure the features from the hand-wrist radiograph and a decision system based on neural network to assess the bone age. The system first made ten measurements by using linear regression analysis to give better correlation coefficients, and finally seven measurements were selected. The weakness of this method is that the system does not use the morphological features applied in the GP, TW, or Fels methods. Hence, there is no major difference between using the neural network method and using the manual GP method for bone age assessment.

2.6.6 Phalanges length- based system

The first version of a fully automated system developed by Pietka, Gertych, and Huange (Pietka et al., 1991) was released in the 1990s based on a Picture Archiving and Communication System (PACS), and uses the digital atlas of radiographs in a controlled manner,). This system applies a rough estimation based on the phalangeal length measurements taken from phalangeal length table prepared by Garn. The system extracts specific regions of the hand-wrist based on rough estimates. For example, if the subject's age is less than eight years, the carpal bone region is selected for analysis.

The image processing techniques and algorithms of the system used to evaluate and retrieve the skeletal features are very simple but time-consuming. The system uses a web-based image distribution approach with a digital atlas using a query language engine. However, this method was introduced as a practical and reasonable computerised method of bone age assessment using applied fuzzy classification to overcome the problems of noisy data and subjective decision.

The fuzzy systems are dependent on the reference population because they link the relationship with age rather than measuring the skeletal maturity, and this is a significant restriction. Therefore, most of the test results released for the system are based on the accuracy of the region of extraction or segmentation. A comparison between the estimated age by the system and the chronological age shows roughly a difference of one year. The method tries to improve the segmentation of the phalangeal epiphyses as well as the analysis of the carpal bone analysis and radial epiphysis by applying Gibbs random with contour model segmentation.

Bone age assessment based on the phalangeal length has always raised the question of what happens to the estimation if the preliminary assessment is inaccurate, and this is the main drawback of this method. Hence, the phalangeal length is not a reliable indicator for skeletal maturity.

2.6.7 The third digit - three epiphyses: Sato et al.

Sato et al. (1999) proposed an automated system to assess the bone age of Japanese children based on the analysis of the bones of the third digit. This system is known as the computer-aided skeletal maturity assessment system (CASMAS).

This method uses the proximal, middle, and distal epiphyses of the third digit based on the width of the epiphysis to the metaphysis, and the width of the metaphysis-epiphysis to the metaphysis, and evaluates the radial epiphysis when the epiphyses is completely developed. Evolution of the system has presented reasonable results for the age range between two and 15 years, but for very young children and those aged above 15 years, the results are not so accurate. This is because the epiphysis is still undergoing development in young children, and it overlaps for older children. To a certain extent, this problem limits the use of this system for bone age assessment.

2.6.8 Phalanges, epiphyses, and carpals

The National Tsing-Hwa University in Taiwan, presented a computer-based system for bone age assessment, similar to the system proposed by Sato et al. (2007), and based on the bones of the third digit. This system, however, involves extracting the left hand image from the X-ray image from both hands on the same radiograph (Hsieh et al., 2007). This method uses the thresholding methods and heuristic searches to rotate the radiograph at the pre-processing stage. The system works on the phalangeal region of interest (PROI) and segments the phalangeal bone with Gabor filters for smoothing, and Canny edge detector as well as local variance method for finding the edge and refining it. The PROI segmentation includes full grey-scale information, and it is a successful method for BAA with low error rate during evaluation.

Two sets of information are derived from the PROI segmentation. The first set contains geometric indicators of length, width, and area of the distal phalanx, and proximal phalanx. Despite the length of the distal phalanx showing low contrast in some X-ray images it has been used to normalize the lengths and the areas. The second set of information includes the information on the shape of the epiphysis and the distal phalanx. These features are fed to the neural network for analysis. The method uses three neural networks for leave-one-out statistical training and testing, including:

a. Back-propagation;
b. Radial basis function; and
c. Support vector machine.

Although the support vector machine produces the best performance among these three networks, its accuracy has been evaluated to be 85%. To decrease the error rate, the system applied the carpal bone information for subjects below eight years using a fuzzy membership function. The carpal bone age is considered as a mask for the output value of the neural network and the final result combines the carpal age result, plus the two outputs above, as well as the two outputs are less than the estimate. If the children are older than seven years, the two largest neural network estimates are applied. The research group improved their method in 2008, by screening children with Turner’s Syndrome using measured bone age and distal-middle phalanx ratio.

2.6.9 Mahmoodi model

Mahmoodi (2000) used computed features. In his proposed automated system based on analysis of the phalangeal region using an active shape model and a knowledge-based technique. The system first conducts a hierarchical search to focalize the bones, then an active shape model is set up by a bone contour. The system extracted three shape features that had 0.72 and 0.89 correlation coefficients with the actual age. These shape features include the moment of the proximal end of the phalanx with the ratio of width of epiphysis to the metaphysis. This method helps to identify the relationship between the epiphysis-metaphysis region and the chronological age. They reduced the risk of inaccuracy in assessing the bone age by using the Bayes risk principle from the decision theory. The system was evaluated using a leave-one-out technique. In this technique, an X-ray image is removed and the system uses the remaining images and trains using the current sample. The removed image is then evaluated as a new parameter. The system achieved 82% accuracy for male patients, and 84% for female patients. They claimed they could increase the accuracy of the system by improving the training sample set.

2.6.10 Neural network classifiers using features of the RUS and carpal bones

Liu et al. (2008) developed a computerized system for bone age assessment using artificial neural network based on two geometric features of the RUS and carpal bones. This system uses a large database of samples and algorithm of particle swarm applied for segmentation of the bones. This method applies two classifiers to estimate the bone age - the RUS bones, and the carpal bone for children aged below nine years. This method has a small standard deviation in the differences when a comparison is made between the system assessment and the observer’s assessment. The strength of this system is that it reduces the variability in the carpal bone-based system compared with other systems.

2.6.11 Neural network based on the radius and ulna

Trist and Arribas (2008) proposed a computer-based system to estimate bone age based on the TW method and using the radius and ulna bones. This system is assisted with manual landmarks and an adaptive clustering technique is then applied for segmentation of the radius and ulna.

The method applies neural networks in the decision-making stage to make a posteriori probability that predicts the error rate - this feature is specific to this method. The range of the mean difference between the system and the observers is large, and hence, this method is limited to only four TW3 levels. However, the researchers claimed that their method could be extended by improving the bone segmentation technique. In this context, the use of a neural network should be considered.

2.6.12 Neural network analysis based on the epiphyses and carpal bones

The common process for assessment of bone age of the hand-wrist bone is to make an outline of the border of the bone and then extract the feature from the outline. For the carpal bone, it is very difficult to find the bone border due to the low contrast at the edges, noise in the X-ray image or overlapping soft tissues. Rucci et al. (1995) stated that they could overcome this problem by using a trained neural network to extract features of the images. This method uses an attention focuser and a bone classifier in a neural network architecture. The attention focuser implements pixel-processing to link a hidden neural network to create an output, which they call X and Y values relating to the centroid of the images of bones. The method was tested using 56 radiographs of low quality and 16 additional images. The results show 65% accuracy and 97% accuracy, respectively, and a standard deviation of 0.85 years. The results provide evidence that the neural network is a useful technique for classification in the TW2 method. Bocchi et al. (2003) improved the system to make it a fully automated method for age estimation. In this method, a user labels specific regions of the bone on the radiograph. The same pixel-processing technique as that used in the Rucci method is used except that it includes analysis of epiphyses.

This manual labeling method indicates an average difference of 0.05 years, and a standard deviation of 0.7 years, between the estimated age and the observer's estimation and an error rate of 1.4 years. The results are acceptable but the age ranges used for testing are not stated, and there is no indication whether the system could be applied to missing data and overlapping bones. The results show that the neural network is a powerful technique for image processing. The main drawback, however, is that the neural network system starts as a dumb state.

2.6.13 The Royal Orthopaedic Hospital Skeletal Ageing System

Hill and Pynsent (1994) described the ROHSAS (Royal Orthopaedic Hospital Skeletal Ageing System) which is based on the 13-bone and 20-bone TW2 method. The system works with an iterative method and finds the outline of the hand, the phalanges, carpus, radius-ulna bone, and take about four minutes to estimate the bone age . This method can also detect the left and right hand using radius and ulna widths. A fuzzy set and an entropy technique is executed for bone segmentation. A shape recognition method is used for bone classification with normal fuzzy and fractional fuzzy grammars, and an octal chain code defined by Kwabwes (1985) specifies the bone edges. The user has the facilities to interpose or ignore the bone classification, if needed, in the CASAS system.

Cox (1994) tested the system with 98 images from the International Children Centre London Longitudinal Study. The results show 0.5 year between the systems, and in 74% of the estimation there was no difference between the estimations by the system and the observer. The system, however, had a 25% rejection rate. As a result, Cox stated that the system is a reliable method for bone age assessment albeit the need for a larger group of sample images including the image of normal healthy children, for estimation.

2.6.14 BoneXpert system

Thodberg (2009) proposed the BoneXpert system is an automated method for bone age assessment. This method is based on the shape-driven active appearance and the TW RUS-based approach (using the radius, ulna, and short bones).

Using the shape and intensity features caused a robust algorithm of the active appearance model in this system. A set of components of more than 3,000 bone contours were rotated and scaled, using the Gobar filters, to form the parameters in the active appearance model. Thirty coefficients were chosen for the features of images using a linear regression technique fed into the active appearance model. Although the usability of the system is still under evaluation, preliminary testing results shows that the performance is reasonable good and that the accuracy is stated as 0.42 years for using the GP method and 0.80 years for using the TW2 method. The system rejection rate was about 1% for poor quality images but it increased to 18% in some cases for the radius and ulna. What is distinct about this method is that it assesses the accuracy of the bone age by using the relationship between the X-ray image and linear growth of the bones. The standard deviation is 0.5 years, which shows an increase in reproducibility calculated using the automated method. The BoneXpert system has been available as a commercial package since January 2009.

2.6.15 Robust processing of carpal and epiphysial/metaphysial bones

Spampinato et al. (2010) presented an automated method for bone age assessment based on the Tanner and Whitehouse (TW2) method and with the integration of two systems: The first system processes the epiphysis/metaphysis region of interest (EMROI), and the second system processes the carpal region of interest (CROI). Both systems use the segmentation technique. The ROIs are extracted automatically and bone age is estimated by combining the gradient vector flow Snakes and the derivative difference of the Gaussian filter. The system was evaluated using 106 X-ray samples and the error-rate is 0.46 ± 0.37 years. This system works for male subject in the age range of 0-10 years, and for females in the age range of 0-7 years.

2.6.16 Web-based bone age assessment for case-based reasoning

A web-based method for bone age assessment was developed by Fischer et al. (2012) for case-based reasoning. The X-ray image of the hand-wrist is first uploaded to the system by the user. The 10 best matching points of the epiphysis, as ROIs, are retrieved and they are presented with their bone age. The extracted ROIs are normalized. The similarity score is calculated by the system and the bone age is assessed by computing the overall bone age estimation from the ground truth associated with each retrieved ROIs. The mean error rate is 0.99 years and the standard deviation is 0.76 years was obtained, and compared with the the mean of the USC-BAA system.

All the methods mentioned as automated methods for BAA, and are briefly compared Table 2.2. Each method has been discussed with reference to the evaluation criteria mentioned in Section 2.5.

Table 2.2: Comparison of automated methods for BAA

Approaches	**Year**	**Inventor**	**Method**	**Advantage**	**Disadvantage**
HANDX System	1989	Micheal and Nelson	Segmentation and isolated	Reduces observation variability	Not very accurate
PROI based-system	1991	Pietka et al.	Segmentation of phalanges and epiphyses	Low mean difference, and error rate	Evaluated on a small scale
The CASAS system	1994	Tanner and Gibbons	Based on the TW2 RUS method	More accurate than manual TW method	Cannot be used for assessing hand-wrist with pathological problems
Middle phalanx of the third finger	1995	Niemeijer	Classifies the middle phalanx of third finger by using the active shape model	Accuracy of 73% to 80% when compared with results from observation.	Method used only in children between age 9 to 17 years.
Neural network system based on linear	1995	Gross et al.	Based on linear distance measures	Better correlation coefficients	Does not use morphological features
Phalanges length based system	1990	Pietka, Gertych, and Huange	Based on a Picture Archiving, Communicatio n System (PACS)	Eliminatedsub jective decision	Depends on the reference population group
The third digit - three epiphyses	1999	Sato et al.	Analyses the bones of the third digit	Reasonably accurate	Used in children between ages 2 to 15 years.

Phalanges, epiphyses, and carpals	1999	National Tsing-Hwa University Taiwan	Based on phalangeal region of interest (PROI)	Low error rate	Poor image processing techniques
Mahmoodi Model	2000	Mahmoodi	Analysis of phalangeal and active shape model	Reduces the risk in assessing the bone age by using the Bayes risk principle	Good potential for further progress
Neural network classifiers using RUS and the carpal bone	2008	Liu et al.	Uses artificial neural network	Small standard deviation of the differences	High image processing loading
Neural network based on the radius and ulna	2008	Trist and Arribas	Uses clustering technique for segmentation	Improves the process in bone segmentation	Limited to four TW3 levels
Neural network analysis based on the epiphyses and carpal bone	1995	Rucci et al.	Pixel-processing linked to a hidden neural network	Useful technique for classification in TW2 method.	Neural network system starts as dumb state
The Royal Orthopaedic Hospital Skeletal Ageing System	1994	Hill and Pynsent	Based on the 13-bone and 20-bone TW2 methods	Reliable method for BAA	Small number of sample images

BoneXpert System	2009	Thodberg	Based on shape-driven and the TW RUS-based method	Highly accurate	Rejects images of poor quality or abnormal structure
Robust processing of carpal and epiphysial/metaphysial bones	2010	Spampinato et al	Based on the Tanner and Whitehouse (TW2) method	A highly accurate, and reliable method	Covers 0–10 years for males and 0–7 years for female.
Web-based bone age assessment for case-based reasoning	2012	Fischer et al.	Based on case-based comparison of ROIs	Highly accurate	Does not assess samples with pathological disorders of the hand

Table 2.2 shows the comparison and the evaluation of 16 automated approaches in bone age assessment. However, some limitations still exist such as low accuracy, unsuitable image processing techniques, and inability of some systems in conducting bone age assessment for samples with pathological disorders of the hand. Next section discusses the main problems in more detail.

2.7 Identification problems and conclusions

Sixteen automated systems for bone age assessment have been discussed. In all system, the usual processes involve of image pre-processing, extraction of RIOs, image segmentation, decision making and getting the result. Figure 2.4 shows a general model for the systems. This is only one simple model based on the review in Section 2.6.

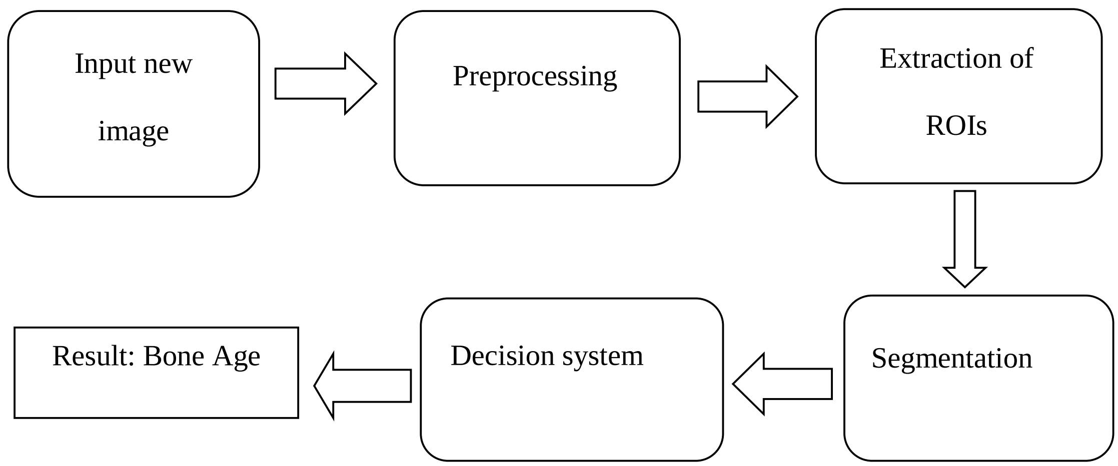

Figure 2.4: A general model of the automated bone age assessment systems

An automated system for the assessment of bone age starts with an input of a digital radiograph of the left hand, or the format digitization of the X-ray images. The X-ray image of the hand is inputted into the system by the user or the radiologist. The pre-processing stage starts after the uploading of the radiograph. In the pre-processing stage, the images are prepared for further analysis, for example, removing the background of the images or rejecting images of low quality.

Most of the algorithms are based on a small set of bones in features analysis and this causes more risk for bone age assessment. Although the region of the bones can be extended, even in normal children, it increases the traffic load in image processing. In addition, the rate of accuracy which is affected by the limitations in the segmentation techniques must be addressed, when legal issues are involved. Current researches on computerized bone age assessment have shown that all the methods concentrate on the technique of segmentation of the ROIs (region of interest).

The basic goal of extraction of ROI level is the parse assessment of bone age into separate stages. Different methods use different regions, such as the carpal bones, phalangeal bones or the radius and ulna epiphyses. The output of this stage is a special region, including the region of interest area in the hand image (O'Keeffe, 2010). The ROI extraction stage, which also involves “image segmentation”, presents the main challenge for the current automated system.

2.7.1 Image segmentation

Image segmentation is a complicated process because there is no standard routine or definition for it, nor is there a unique standard method for its implementation (Pratt, 2001). The segmentation process is defined to separate the specific region of other regions of the hand, and is performed based on the different attributes in the X-ray image, such as intensity or bone texture. The segmentation process is implemented by a contour of bone edge or bone region. The performance of this contour is variable based on the extracted features. This is the reason why a number of algorithms for processing hand-wrist images have problems with the segmentation of special regions in the X-ray image. Moreover, the lack of sufficient image pre-processing techniques causes low accuracy in assessment of bone age (Gertych et al., 2001; Pietka et al., 2001).

Another challenge faced with the current automated BAA systems is that it focuses on the left hand-wrist bones of a normal hand. Hence, there is no solution in forensic cases where there might be defects in the hand because of various reasons incidents, injury or even growth abnormalities (Fischer et al., 2012).

There have been no reports in the literature pertaining to the role of other bones in skeletal maturity, hence, no automated solution has been developed for noisy images or missing data in radiographs of the hand for any reasons for the radiologists.

As a result, this research was undertaken to address the afore-mentioned issues.

2.8 Combined method for improving the automated system for bone age assessment

Although there have been a large number of researches on the automated assessments of bone age, especially those based on the TW method, they are in still at experimental stage and a lot of work is still needed. A major drawback, as mentioned in Section 2.6, is the lack of research on the role of other bones in the BAA system, and how information or data on these bones can contribute in respect of the missing data that could be useful in an automated method of age assessment.

It remains unclear whether the use of other bones in the body in the computerized BAA method can be helpful for radiologists to address the problems of missing data or noisy hand radiographs or when the image of the hand is not available for any reason, in forensic investigation. There are a number of other reference atlases that are available for assessment of bone age for forensic purposes, such as the atlas for the elbow, foot-ankle, knee, pelvic bones, and the clavicle.

One of the objectives of this study is to develop an automated method for bone age assessment for forensic propose based on the hand-wrist bones and the clavicle. The goal is to integrate this analysis of those two bones into one BAA system.

The motivation for this study is based on the hypothesis that an automated system for BAA will remove the observer's variability in bone age assessment process, and make the measurement of skeletal maturity more objective. Furthermore, this combined method can improve the accuracy compression of the systems as discussed in Section 2.5.

The second contribution of this research is that the proposed system is a new solution for forensic cases where there is a missing data or noisy images in the hand-wrist radiographs, and also includes cases of unclear images of hand bones due to abnormalities, trauma, unexpected injury, accidents or congenital abnormalities.

The last section in chapter 2 discusses the study of the combined method for assessment of bones age, and how it can help to achieve the objectives of this research.

2.9 Bone age assessment using a combined approach

Groupon Forensic Age Diagnostics in Germany advised that forensic age estimates should be applied based on combined evidences to obtain more confident result, for example, using X-ray images of the left hand or teeth examination or physical examination to ensure that a subject has reached to the legal age or he/she should be considered to be a minor.

There is no fully acceptable method for age assessment, hence, it is suggested that a combination of various methods with low error rate can be used. Nevertheless, more researches must be conducted on the use of a combination of methods to achieve more accurate results in forensic age estimation (FAE) (Dunkel et al., 1997).

Schmelinget et al. (2001), stated that the combined approach, which uses images of the left hand and medial clavicle, and involving people aged over 18 years is a suitable method for estimation a person's age. The result produced should be accurate enough for submission in the court of law.

Shirley and Jantz (2010) stated the medial clavicle is used extensively in forensic age estimation of young adults because they form a large proportion of the population in forensic casework. Moreover, the clavicle provides a good sample for examination and study of skeletal growth.

Additionally the clavicle is useful in both archaeological science and forensic practice because it remains intact even after being buried for a long time. Hence the medial clavicle has been confirmed as an important indicator for age estimation, for the living as well as the dead persons.

2.9.1 The role of the clavicle in bone age assessment

The clavicle is the first bone in the fetus to ossify with membranous tissues, and as a long bone, it contains a medullar cavity. The clavicle bone has two centres of ossifications. They are : the medial and lateral centres that form from the fifth week of intrauterine life, and are completed during the fetal period itself (Geserick et al., 2000).

Webb and Myers (1985) suggested that the growth of the medial clavicle could be a good indicator in forensic age estimation in both living and dead people. Their research involved a large number of samples revealed that the time of the development of the epiphyseal tissues in the medial clavicle and the union of clavicular shaft, can be used for identification of bone age.

The cartilage starts to grow after the osteoid matrix in the clavicle is complete and this results in the union of endochondral ossification and membranous ossification. About 80% of the bone length of the clavicle is included in the medial cartilaginous mass rather than lateral mass (Scheuer & Black, 2000).

When two ossification centres in the clavicle join in the spatial position at the end of the bone, a special s-shape will be formed continuously from the eight to the nine week of infancy. The bone reaches its complete form during the 11th week of infancy (Ogata & Uhthoff 1990) then its development slows until the fifth year, followed by a big jump in growth after the seventh year and again it slows until puberty. At the age of puberty, the second centre of ossification is at the medial and lateral ends of the clavicle.

Tod and D’Errico (1928) studied the fusion of the medial epiphysis in 20th century samples, but there is still not enough research on the role of the clavicle in estimation of bone age.

Medial epiphyseal ossification starts during puberty, although it does not complete to the shaft is not complete until 10 years from its first appearance (Kreitner et al., 1998).

The medial clavicle bone has been confirmed to be a suitable indicator for bone age assessment in adults. Initially, it is like a tiny spot of bone in the centre and it gradually extends to fill the entire medial surface. Scheuer and Black (2000) classified the period of maturation of the clavicular bones into three stages: The first stage occurs from the age of 16 to 21 years with the appearance of a well-defined medial clavicle flake; the second stagel occurs from the age of 24 to 29 years with most of the medial surfaces filled by flake, and the last stage occurs from the age of 22 to 30 years with complete fusion. Szilvassy (1977), from Australia, also presented the same classification, without any overlapping: the first stage occurs from the age of 18 to 20 years; the second stage occurs from the age of 21 to 25 years with active fusion; and the final stage occurs from the age of 26 to 30 years, when fusion is complete.

Singhe and Chavali (2011) stated that the clavicle bone, in comparison to other long bones in the body, takes the longest time to grow in humans, so its predictive value can be considered to be an effective and credible indicator for bone age assessment during the 30 years when other bones will have been inactive in human life.

In addition, among the long bones in the body, the clavicle bone is the last to fuse and has various developmental levels, thus, it is a valuable indicator of the age at death during the post-pubertal period.

2.9.2 Using the medial clavicle bone for age diagnosis: The manual approach

Stevenson (1924) conducted the earliest study on the medial clavicular bone in Americans. His study was based on the samples of the Hamann-Todd's study. He defined the beginning stage of bone union to be at age of 22 years, and complete union at the age of 28 years, for all samples. He did not observe any difference in the epiphyseal union between males and females.

Todd and D'Errico (1930) conducted a comprehensive study on the medial and lateral clavicle epiphyses. They scored the clavicles based on four phases: phase 1 as no union, phase 2 as beginning of union, phase 3 as a recent union with a scar, and phase 4 as complete union. They stated that unions are formed from age 18 to 29 years. The ossifying centres start to unite from age 21 years and the union would be complete around age 25 years. They did not mention any differences between the genders and race in their study.

McKern and Stewart (1957) released their study on epiphyseal union in 1950 based on the deads from the Korean war. Their report was based on a 5-phase scoring method. They added a phase to the Todd and D' Errico's approach for active union: phase 1 for no union, phase 2 for beginning of union, phase 3 for active union, phase 4 for recent union, and phase 5 for complete union. They found age 18 or early 17 years to be period for the beginning of union and age 25 years for complete union. Their samples were selected from males, hence they did not make any differentiation on sex.

Webb and Suchey (1985) provided a standard reference of a modern sample for forensic purpose. Their study was based on 800 autopsy samples from Los Angeles in the 1970s. They scored the bones after extracting and cleaning them. Their method was based on a 4-phase scoring method but was different from the previously mentioned method: phase 1 is defined as non-union with no epiphysis, phase 2 as no union but with separate epiphysis, phase 3 as partial union, and phase 4 as complete union.

Phase 1 continues to age 25 years for males and, age 23 years for females; phase 2 is from age 16 to 22 years in males, and from age 16 to 22 years in females; phase 3 is from age 17 to 30 years in males, and from age 16 to 33 years in females; and phase 4 is from age 21 to 31 years in males, and from age 20 to 34 years in females, for complete fusion.

Black and Scheurer (1996) introduced a 5-phase scoring system for the medial clavicular based on the skeletons from the 18th century population in Lisbon. Their 5-phase scoring system focused on the non-union phases, as shown in Figure 2.5:

Phase 1: Ossification centre is not visible (not yet ossified);

Phase 2: Ossification centre is visible (no epiphyseal flake attached);

Phase 3: Growth plate is ossified, partially (flake commencing fusion);

Phase 4: Complete union of the epiphysis and metaphysis (fusion line is still visible) ;

Phase 5: Complete union (No trace of a fusion line).

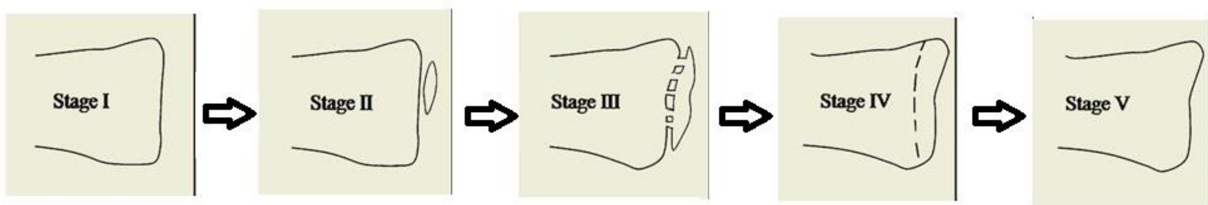

Figure 2.5: Five phases for bone age determination

Phase 1 was observed from age 11 to 17 years, phase 2 from age 15 to 22 years, phase 3 from age 19 to 23 years, phase 4 from age 23 to 28 years, and phase 5 from age 25+ years. The age ranges did not differentiate between the male and female samples because of the small sample size.

In summary, the clavicle epiphysis has been considered to be a useful and reliable indicator for skeletal age estimation in adults. Despite the different scoring methods used in current researches, there is no standard scoring method that also defines the accepted error rate. This research uses the clavicle bone as a combined approach with the hand bones to determine the bone age in forensic cases where there is problem in assessing the age using X-ray images of the left hand.

2.9.3 Summary

Section 2.8 discussed the use of a combined approach as a reliable method in bone age assessment (BAA). The various studies have shown that the use of the combined method in BAA produces more accurate estimation of bone age. The potential benefit of the combined system is that it allows more reliable decisions to be made on bone age, and thus, more accurate estimation of age of people, which could not be determined earlier.

The clavicle bone is selected for developing the combined method beacuse it is considered a useful bone for age assessmnet among members of the forensic community. The clavicle bone is considered a long bone in both in forensic practice, and in anthropological and archaeological studies because it remains intact even being buried for a long time (because of its highly compact). It is also suitable ageing bone for assessing the age of young adults (Singh & Chavali, 2011).

2.10 Conclusions

1. The review on automated methods for bone age assessment (BAA) has revealed two fundamental problems to be addressed:

   1.1 The computerized system for bone age assessment based on the hand-wrist reported in the literature highlighted the problem of segmentation of the region of interest (ROI) in the hand images. Furthermore, lack of appropriate image processing techniques has resulted in low accuracy in bone age assessment.

   1.2 Current automated methods for bone age assessment ignored the role of the other bones in young adults, and as well as in handling forensic cases where defects and other abnormalities and injuries on the hand are present. Presently, most systems handle only X-ray images of the left hand of normal samples.

2. In view of the previously-mentioned problems and shortcomings the following issues need to be addressed:

   2.1 There is a pressing need for a new computerized system that uses the combined method for age estimation to overcome the current limitations and to perform better overall than existing methods.

   2.2 The clavicular epiphysis is an important bone in forensic investigation, and the combined use of the hand bone with medial clavicle bone can provide suitable indicators for age estimation, and that is the acceptable result to be submitted before a court of law.

Chapter 3: Research Methodology

3.1 Introduction

Chapter 3 discusses the research design and the methodology used in this study to answer the research questions and to achieve objectives of the research, as outlined in Figure 3.1. In the context of this research, both qualitative and quantitative research methods are used (Tashakkori & Creswell, 2007).

Information is gathered from the targeted respondents using a questionnaire as well as through interviews and observational. The research methodology is implemented in seven steps, as follows:

- A review of the literature pertaining to BAA;
- A questionnaire survey to investigate the current methods for BAA used in University of Malaya Medical Centre (UMMC);
- Interviews with experts in radiology and orthopaedic surgery pertaining to BAA;
- Observational study;
- Analysis of collected data;
- Design and implementation of the BAA system;
- Evaluation of the accuracy and usefulness of the BAA system

The next section will discuss the reasons for collection of data from the Faculty of Medicine in University of Malaya Medical Centre (UMMC).

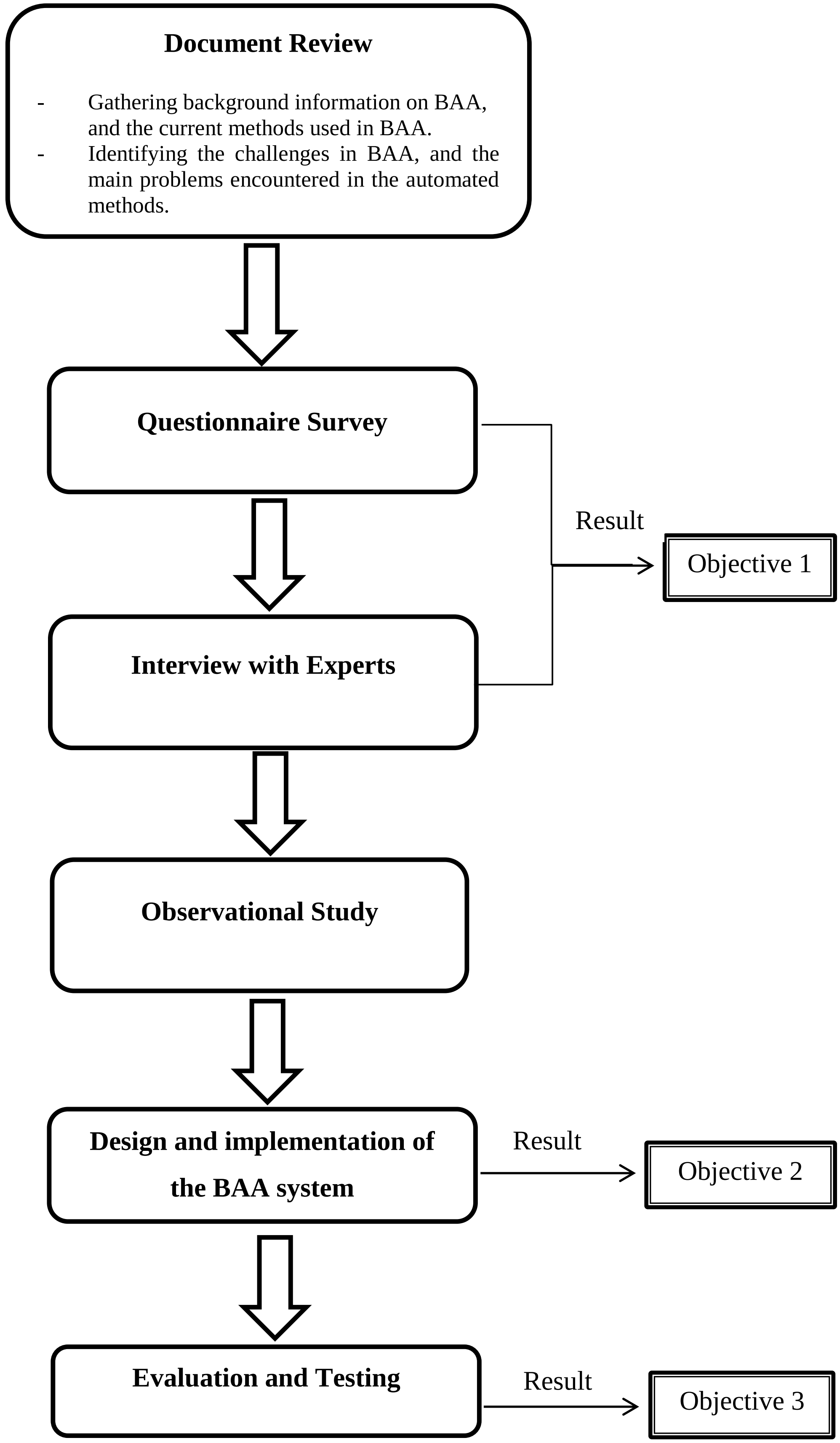

Figure 3.1: Research framework for thesis

3.1.1 Faculty of Medicine of UM as the Focus Environment in Research

Data collection was carried out in the University of Malaya Medical Centre (UMMC) because it has specialists in the area of bone age assessment (BAA). The eforts were made to involve other institutions through online application to the related website (“https://www.nmrr.gov.my/fwbLoginPage.jsp?fwbPageId=NMRR_Home”) as well as going to the Forensic Center located in Kuala Lumpur, but these efforts were unsuccessful.

The Faculty of Medicine, University of Malaya, located at the Lembah Pantai Campus, was established more than 50 years ago. UMMC has been in the forefront of the postgraduate clinical training and education, and thus, has a wide range of medical specialties programme at Masters and PhD levels. This medical centre housed the first medical school in Malaysia, and currently provides excellent training facilities for both undergraduates and postgraduate students in all fields of medicine to fulfill its mission of achieving excellence in patient care, education, and research (http://medicine.um.edu.my/).

The faculty has 14 departments. Most of the information needed in this study was gathered from the Department of Biomedical Imaging (formerly the Department of Radiology). This Department, located on the 2nd floor of the Menara Utama of the UMMC was established in 1964. The Department has about 300 staff members, including both academic and non-academic staff, with Professor Madya Dr. Yang Faridah Binti Abdul Aziz, as the Head of Department.

Collecting data using both the survey questionnaire and interview in parallel was one of the main challenges faced in this research. To obtain permission for gathering information from UMMC, the researcher had to perform Medical Ethics Application Standard Operating Procedure (SOP). The researcher had to fill in an application form to conduct her research project from the following link:

http://www.ummc.edu.my/index.php (Refer to Appendix F), and provide other related documents such as the research proposal, CV, Study Protocol, Consent Form, Patient Information Sheet, and submit them to the UMMC Medical Ethics Committee, in September 2012.

In October 2012, the researcher had to present her proposal in the Faculty of Medicine in the presence of Professor Ng Kwan Hoong and Assoc. Prof. Kartini Rahmat, two members of the Scientific Committee of University of Malaya Research Imaging Centre. After passing the mentioned session and getting the approval from the Department Biomedical Imaging, in order to get the final permission to collect data, the researcher defended her proposal in the presence of the main members of Medical Ethics Committee of UMMC on 28th November, 2012.

Finally, on 24th January 2013, the committee approved the proposal and also gave permission to collect data from the Faculty of Medicine, University of Malaya (UM).

3.2 Information gathering 1: the questionnaire survey

Although bone age assessment has become an important subject of academic interest today, but there still exists some problems. A major problem is that traditional methods produce low accuracy and low consistency in assessing skeletal maturity (Fleshman, 2001). Hence, this study aims to develope a new approach to assist radiologists and forensic experts in making more accurate assessment of bone age.

A questionnaire is designed to obtain feedback on the current methods used in UMMC for bone age assessment, the problems encountered, the drawbacks about the current methods used, seek opinions about new approaches that can be used, and to identify the requiements needed to develop a new method for BAA. In view of the difficulty in contacting the busy medical staff, the questionnaire is the easiest method to use for collecting the data. The researcher tried to design a simple questionnaire that needs little time and effort to answer, in order to encourage the respondents to answer all the questions (Schonlau et al., 2002). The survey questionnaires (Appendix B) were distributed to the postgraduate students (Master's students) in radiology, studying in the Department of Biomedical Imaging, UMMC.

3.2.1 Collection of data

In this research, a survey questionnaire was used for collecting the data required from UMMC and the radiologists in the initial phase of the research because of the following reasons:

i. Usually, directing questions to the expert respondent is useful in overcoming the limitations of single source (Premkumar & King, 1992).
ii. Distributing the questionnaire to the knowledgeable population saves the time to achieve the main objective.

The information was collected through the survey questionnaire from the Department of Biomedical Imaging, of the Faculty of Medicine. Self-designed questions were distributed to the radiologists. This survey questionnaire was the primary source of collecting data at the initial phase of this research.

3.2.2 Questionnaire design

Several changes were made to the questionnaire before it was distributed to the target population (Mansourvar et al., 2014). The survey questionnaire includes two general sections: Section A and Section B. The first page of the questionnaire contains the title of the study, and brief description of the objectives. Section A is divided in to five parts. The first part is to gather personal information on the respondents and covers general information such as level of education and age. The second part is concerned with the level of experiences of the respondents in BAA, and his/her proficiency in BAA, and the method used in assessment of bone age.

The third part consists of questions to evaluate the current status of BAA in UMMC, the reasons for using BAA, the time spent in BAA, and the problems encountered. The fourth part deals with factors affecting in bone age assessment. Finally, the fifth part solicits feedback on identifying the alternative choice for radiologist when using images of low quality like noisy or missing images. Section B of the questionnaire contains questions on the significance and motivation for designing and developing an automated system for bone age assessment. This section includes six questions which can be answered using a Likert-like scale ranging from 1 for strongly disagree to 5 for strongly agree . Table 3.2 presents the type of questions (column 1) and the reference to the sources from where they were taken.

Table 3.1: The structure of survey questionnaire

Section A	**Questions**	**Literature**	**Hypothesis**
Part1	Personal Information	Lequin et al. (2009)	To identifty the general information of respondents, academic level of study, gender and sex.
Part 2	Experience Level	Lequin et al. (2009)	To elicit information on the proficiency level of respondents in BAA.
Part 3	Evaluation Current Method	Berst et al. (2001) and Garamendi et al. (2005)	To evaluate the method used in UMMC for assessment of bone age, and identifying the criteria and problems.
Part 4	Effective Factors	Scanderbeg et al (1998)	To discover the factors such as race or sex that can affect estimation of bone age.
Part 5	Alternative Selection	Grundmann et al. (2008)	To identify the alternative choise for radiologist in facing problem of low quality images or noisy images.
Section B	**Questions**	**Literature**	**Hypothesis**
1 to 6	Motivating Factors in automated BAA	Mansourvar et al. 2012	To identify motivational factors that can influence radiologists to use automated method for BAA.

The questionnaire was carefully designed because the respondents were from the Faculty of Medicine. The researcher pretested the questions with her supervisor and one radiologist before starting the actual survey. The use of a paper-based questionnaire is a traditional method for collecting data.

3.2.3 Analysis of data

This research could be considered exploratory in nature as this is a new area in forensic science and medicine. In addition, there is little existing background information on the topic of this research. The SPSS software version 21 for Windows was used for analyzing the collected data.

3.3 Information gathering 2: the interview

According to Lewis (1998), document review, data and intuition are the basics of the theory and methods for the development of model. In addition, the combination of these three techniques forms a model for high quality research. With the knowldge obtained from reviews of ducuments, as defined in Chapter two, the researcher decided on using the following methods for this study.

With the goal of achieving further understanding on the process of data collection for this research, interviews were conducted with the doctors, especially the specialists in the radiology and pathology from the Faculty of Medicine, University of Malaya (UM). Six persons from Depertment of Biomedical Imaging and Orthopaedic Surgery were interviewed to find the answers to the research questions.

3.3.1 Collection of data

The interview questions were designed based on the research conducted by Berst et al. (2001) to identifty the factors that can affect bone age, the main problems and limitations in making assessment of skeletal age. Additional questions to identify the interests of respondents in BAA and the factors that motivate them to use automated method for BAA (Refer to Appendix C).

This study used a structured interview because of the respondents in this project (Mackenzie & Knipe, 2006). It means that the researchers asks a predetermined set of questions using the same words, and in the same order and with a special interview schedule. The benefit of the strucured interview is that it collects uniform knowledge in the related research area, leading to the comparability of the information. Although the unstructured inteview is more flexible, the structured inteview needs fewer interviewing skills.

To collect data through an interview, the researcher prepared a set of nine questions for the doctors from the Faculty of Medicine, UMMC. Twenty emails messages were sent to professor, senior lecturers, and lecturers who are specialists in radiology, and pathology to request for an interview time. Only three out of twenty emails were answered, and the interview time was given in advance, and three doctors agreed to the interview when they were approached by researcher, directly. Furthermore, interview as qualitative research is much more subjective than quantitative research. Hence, because of nature of this type of research small numbers of people are interviewed in-depth and a relatively small number of focus groups are conducted (Judge et al., 2002).

The interview was held in UMMC over two weeks in February 2013. The respondents who agreed to attend the interview were the staff from the Department of Biomedical Imaging and the Department of Orthtopaedic Surgery, as the follows:

1- Prof. Dr. Saw Aik **(**Department of Orthopaedic Surgery)

2- Associate Prof. Dr. Kartini Binti Rahmat **(**Department of Biomedical Imaging**)**

3- Dr. Caroline Judy Westerhout **(**Department of Biomedical Imaging**)**

4- Dr. Roshan Gunalan **(**Department of Orthopaedic Surgery)

5- Dr. Anis **(**Department of Biomedical Imaging**)**

6- Dr. Alireza Shademan **(**Department of Biomedical Imaging**)**

3.3.2 Interview design

The interview questions are divided to three parts:

1- The first section contains three primary questions - the main method used for bone age assessment (BAA) in University of Malaya Medical Centre (UMMC); the current problems and limitations; and the maximum or minimum errors rate in BAA.

2- The second part investigates the alternative technology for BAA; and

3- The third part involves questions six to nine on the importance of an automated system for bone age assessment, requirements and features of a computerized system.

Table 3.3, below, shows the interview questions posed to the respondents. The details results of the interview will be explained in Chapter 4.

Table 3.2: The Structure of Interview Questions

	Question 1	Question 2	Question 3
Part 1	What is the main method for bone age assessment in UMMC?	What is the maximum and minimum error rate?	What are the main problems in the current method?
Part 2	If you do not use the left hand image, what do you use for bone age assessment?	Which bone do you prefer to use to assess bone age and which one has less error? (Elbow, knee, clavicle, pelvic , …., etc)	Do you think it is essential to have an automated system for bone age assessment to replace the manual method?
Part 3	Which method do you prefer? Manual or automated	Which features are important for developing a computerized system?	Do you prefer a web-based system or stand-based system?

3.3.3 Analysis of data for interview

The analysis of the interviews shows the common techniques that experts used for BAA in UMMC. The results provide the background information required by doctors for bone age estimation in children and is explained further in Chapter 4. The interview feedback, would be used to identify the requirements and features for an automated system to assist the radiologists in assessing bone age.

3.4 Information gathering 3: Observational Study

The observational study is a type of research method that allows the researcher to observe in a systematic way, the behaviour and manner of working of people in an environment. An observational study could be of two types: naturalistic observation, and laboratory observation. In naturalistic observation, the researcher records the behaviour in the natural environment, while a laboratory observation takes place in a laboratory environment (Pronovost et al., 2010). Laboratory observation is used in this study.

The venue of the observational study was an X-ray lab in the Department of Biomedical Imaging - a place where the radiologists review the results of radiological tests or other diagnostic imaging procedures. The aim of the observational study is to acquire a full understanding of the radiologist's behaviour and how they carry out bone age assessment procedure at UMMC.

There are seven questions for the observational study (Refer to Appendix A), complied from the analysis of the interviews with the relevant medical experts in UMMC and from the information that gathered from the documents reviewed. The seven objectives for the questions are as follows.

1- Background information of respondent

It is to find out the demographic background of the respondent, and her knowledge and experience in BAA.

2- Use of BAA technique in UMMC

It is to obtain information on the history of the BAA procedure in UMMC, and issues pertaining to its implementation such as the time and period of training the radiologists on BAA.

3- Common method for BAA at UMMC

This question is aimed at finding out how BAA is implemented in UMMC.

4- The reasons for conducting the BAA procedure

It is to find out the main reasons for implementing bone age assessment procedure in UMMC.

5- Identify the problems encountered in BAA

It is to find out the problems that radiologists faced when conducting BAA in UMMC.

6- Investigate the frequency of conducting BAA

It is to find out the how often the radiologist in UMMC conduct BAA.

7- Significance of using BAA

It is to find out the significance of using BAA.

The observational study was conducted over two weeks in February 2013, and consisted of two sessions. The researcher sent the questions (Refer Appendix A) to the respondent, and observation started in parallel with the questionnaire study in February 2013, and it involved a radiologist from the Department of Biomedical Imaging. Observation study as qualitative research is much more subjective, hence, a small number of groups are conducted (Judge et al., 2002).

3.5 Design and implementation of BAA system

The Bone Age Assessment system in this research was designed based on the use of the following X-ray images, together:

- Hand/wrist images; and
- Clavicle images

A bone age subsystem1 called **BAA1** was obtained from the radioghraphs of the hand-wrist, and a bone age subsystem2 called **BAA2** was obtained from clavicle X-ray images. BAA1 and BAA2 are integrated into a final BAA system that can be used in the forensic environment. This research uses the Analysis, Design, Development, Implementation and Evaluation (ADDIE) model for the system development methodology.

Chapter 5 will present the detailed information on the designing, implementation, and programming part of the research. The discussion in Chapter 5 is based on the findings from Chapter 2 to Chapter 4. The preliminary framework for bone age assessment system is proposed in Figure 3.2.

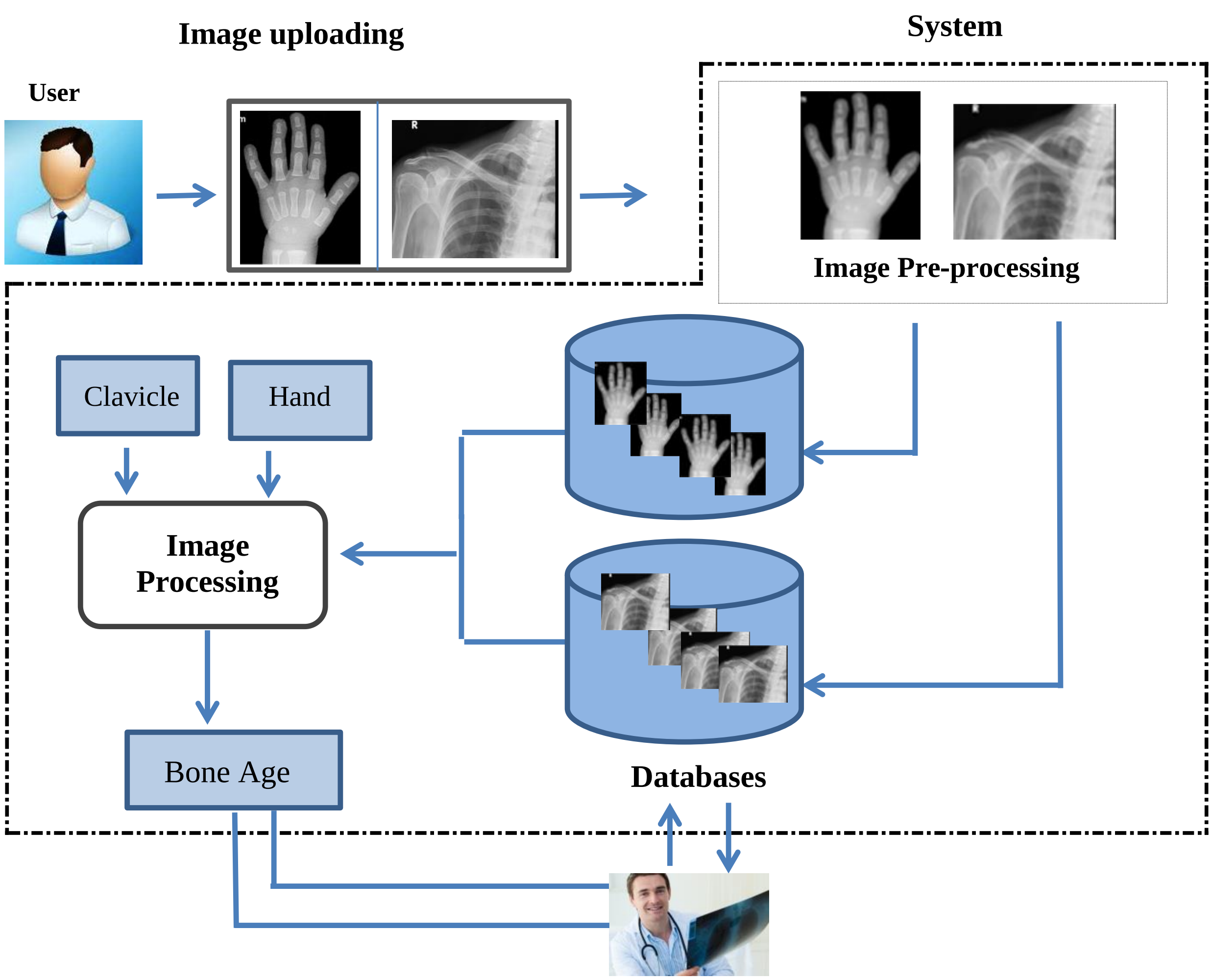

Figure 3.2: Framework of BAA system using hand and clavicle bones

The proposed framework for BAA based on using the hand bone and the clavicle bone involves four main concepts: user-interface, database, image preprocessing and image processing, as further explained in Chapter 5.

3.6 System evaluation

3.6.1 Methodology of evaluation

Three different tests were carried out to analyze and evaluate the accuracy and usability of bone age assessment (BAA) systems (see Figure 3.3). The integrated BAA system that combines the use of the hand and the clavicle bones was conducted on separate set of data. Test 1 is divided into three sub-sections to evaluate the accuracy of BAA1 subsystem based on the hand-wrist images. In the first sub-test, the data is divided into eight parts by race and gender. In the second sub-test the data is classified into two sections - male and female - both categories include four races. The third sub-test involves an universal data mixed with the race and sex. Test 2 is conducted to evaluate the accuracy of BAA2 subsystem to test the performance of bone age assessment method using images of the clavicle. Test 2 divides the data into two categories - left and right radiographs. Test 3 is conducted to examine the usability of the whole system that integrates BAA1 and BAA2. Test 3 contains a set of questions divided into five sub-scales or attributes : Affect, Efficiency, Helpfulness, Control, and Learnability. Test 3 follows the SUMI standard method, which is used to measure software quality from the end-users point of view (SUMI, 2008).

3.6.2 Statistical analysis

A paired *t*-test for the above sub-tests was applied to test 1 and test 2. The difference between chronological age (CA) and bone age from the system was calculated . The mean value, standard deviation (SD) of CA and BA system and their difference (CA-BA) was considered for separate sub-test systems.

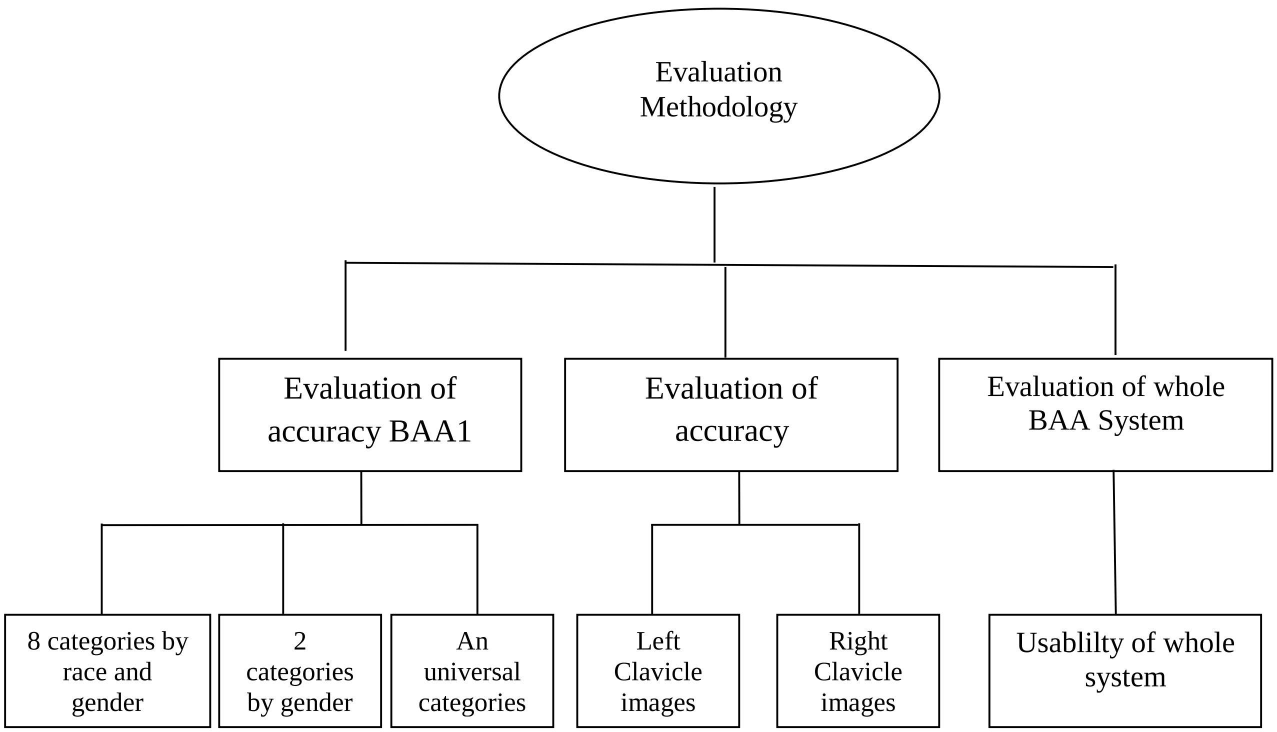

Figure 3.3: Methodology of Evaluation of BAA System

3.7 Summary

This chapter explained the methodology of this research. It includes the following steps:

1) Documents review that is the starting point of this study.
2) A questionnaire survey to investigate the current method of BAA in the University of Malaya Medical Centre (UMMC)
3) Interview with the experts

4) Observational study
5) Analysis of the results
6) Design and implementation of BAA system
7) Evaluation of accuracy and usability testing of the BAA system

Based on two main methods for collecting data - survey questionnaire and interview - the research questions were identified and the first objective was achieved. The targeted populations for this research were the medical people from the Faculty of Medicine, in UMMC.

Collection of data in this research leads to find the information on the designing and developing of a new BAA system based on the hand and the clavicle X-ray images.

Chapter 4: Data Analysis and Findings

4.1 Introduction

Chapter 4 discusses the results obtained from the analysis of the quantitative and qualitative data. The Faculty of Medicine, University of Malaya Medical Centre (UMMC) was the scope for this study because of two main reasons: (1) UMMC is involved in bone age assessment as one of its clinical service to patients (see observational study in Chapter 3). Patil et al. (2011) mentioned that assessment of bone age is regularly carried out in hospitals to examine physical growth of children and adults, manage limb length discrepancies, conduct research on endocrine diseases, and peadiatric defects and disorders; and (2) It was the only center to give the permission for data collection for this research in comparison to the other health clinics or forensic centres.

This chapter will also discuss the analysis of the data obtained from the questionnaire survey as well as interview with the experts from UMMC. The results from the analysis will give a clear understanding of the status of BAA in the UMMC, the significance for doing BAA, the challenges faced, the reasons for conducting BAA, the problems that radiologists faced in BAA, and the motivating factors that led to the development of an automated BAA system.

4.2 Findings of the survey

The first part of this section presents the findings of the questionnaire survey, which was conducted to achieve the following objectives:

1. To identify the method used for bone age assessment (BAA) in the University of Malaya Medical Centre (UMMC);

2. To identify the factors that can affect the assessment of bone age; and
3. To investigate the motivating factors that influence radiologists to express their desire for an automated system for bone age assessment.

The survey questionnaire consists of two main sections: Section A is divided into five parts - Part 1: to elicit the personal information of the respondents; part 2: to identify the experience level of the respondents in BAA; Part 3: to evaluate the method used for BAA in UMMC; Part 4: to identify the factors that that can affect decision-making of the respondents in assessing bone age; and Part 5: to identify what alternative solutions are available to respondents when they are faced with the unusual cases. Section B deals with factors that motivated the development of an automated system for bone age assessment in the clinical environment.

4.2.1 Respondents

The collection of data through the survey questionnaire was carried out in the first three weeks of February 2013. The questionnaire was distributed to 55 selected respondents in the Faculty of Medicine, University of Malaya. The questionnaires were distributed during the break time in the classes for postgraduate students in radiology in the Department of Biomedical Imaging. The respondents were selected because of their experience and knowledge in BAA. The completed questionnaires were collected after the class was over. Of the 55 questionnaires distributed, only 36 questionnaires were fully answered. This shows a 65.5% response rate and this could be considered to be satisfactory. Pearlson and Saunder (2004) stated that a response rate 20% to 50% is acceptable. Furthermore, Kearns and Ledere (2004) stated that in the survey of elderly people, generally, lower response is recorded.

4.2.3 Data analysis and results of questionnaire survey

Data is analyzed using the statistical software, SPSS 21.0 for Windows, as mentioned in Chapter 3. The results are discussed in detail in the sections, below. The data was collected from the returned questionnaire, and the process of recording and analysis took five days.

4.2.3.1 The personal information

The data collected on the respondents include the year of study, gender, and age, and shown in Tables 4.1- 4.3. Thirty-six respondents (19.4%) are either in the first year or second year study in the Master's programme, while the majority of the respondents (47.2%) are in year three, and followed by 13.9% of respondents who are in year four.

On the gender distribution, 72.2% are females and only 27.8% are males. Table 4.3 shows that most of the respondents (91.7%) are radiologists between the age of 30 and 39 years, and only three of them are between the age 20 and 29 years. The analysis of demographic information indicates that the respondents are adult experts in BAA, as most of them are Master of Radiology in year three. As mentioned in the observational study discussed in Chapter three, the radiologists are trained in BAA from the first semester of the postgraduate course. The next section discusses the respondents experience in BAA, based on their feedback to the questionnaire.

Table 4.1: Respondents' academic's Year of Study of

Year Of Study	Frequency	Percentage (%)
Year 1	7	19.4
Year 2	7	19.4
Year 3	17	47.2
Year 4	5	13.9
Total	36	100

Table 4.2: Gender distribution of respondents

Gender	Frequency	Percentage (%)
Male	10	27.8
Female	26	72.2
Total	36	100

Table 4.3: Age of respondents

Gender	Frequency	Percentage (%)
19 and below	0	
20-29	3	8.3
30-39	33	91.7
40-59	0	0
Total	36	100

4.2.3.2 Experience level of respondents in BAA

Table 4.4 shows that the majority of respondents (80.6%) have two to three years of experience in BAA. Five respondents (13.9%) have less than one year experinece, and two respondents (5.6%) have four years of experinece and none of the respondents has more than 5 years experience in this field. This analysis of the data confirms the data shown in Table 4.1 which shows that most of the respondents are in Year three of their study. When the respondents were asked how long does it take to become an expert in bone age assessment using X-ray images, 33.3% confirmed they take two to four months, and another 33.3% said that it takes four to six months, while 16.7% of respondents stated they need one to two months, or from six to twelve months (Refer Table 4.5). The answers to this question indicate that time to acquire enough experience and skill in BAA varies among radiologists, and it could be from a minimum one month to one year.

The last question regarding the atlas which the radiologists use for conducting BAA in UMMC, all respondents answered that they use the Greulich and Pyle (GP) method and the accompanying atlas. This supports the finding in the observational study (Chapter 3) which indicates that the GP atlas is preferred by the doctors and experts in BAA. This method is also the most preferred method in United State based on the findings of Zerin and Hernandez (1991). In the survey conducted by Buckler (1983) on pediatricians in Wales and England, however, it was found that the Pyle atlas is the preferred atlas used for BAA.

Table 4.4: Working Experience in BAA

Year Of Experience	Frequency	Percentage (%)
Less than 1 year	5	13.9
2 years to 3 years	29	80.6
4 years to 5 years	2	5.6
More than 5 years	0	0
Total	36	100

Table 4.5: How long does it takes Become an Expert

Time to become expert	Frequency	Percentage (%)
About 1 to 2 months	6	16.7
About 2 to 4 months	12	33.3
About 4 to 6 months	12	33.3
About 6 to 12 months	6	16.7
Total	36	100

4.2.3.3 Evaluation of current method

Table 4.6 shows the number of BAA cases that radiologists handle in a week. Twenty-eight (78.9%) respondents said that they handle from five to ten cases, and eight (21.1%) respondents said they handle from 10 to 20 cases. The feedback shows that BAA is a part of the daily task for the radiologists in UMMC. The specialists in this field should handle at least one BAA case per day.

Berst et al. (2001) stated that there are many reasons for conducting BAA. Table 4.7 shows that in UMMC, the main reasons for using BAA are for diagnosis of growth disorder, and estimation of height (11.1%), and treatment using growth hormone (8.3%,).

Gilsanz and Ratib (2005) stated that the evaluation of skeletal age is important for the identification of growth disorders that could be categorized into two global groups based on distinct etiologies, prognoses or therapies. Initial growth disorder is caused by inherent defects in the skeletal growth process. For example, bone dysplasia could be due to an inherited defect or even prenatal problems that result in the reduction of diaphysis without essential delay of epiphyseal maturation. Therefore, during the period of growth, the potential normal skeletal growth is affected, although skeletal age is not postponed or is postponed much less than the height.

The second group of growth disorder concerns factors outside the skeletal growth process, which can adversely affect epiphyseal or even osseous maturation. These factors could be nutritional, or metabolic factors, or other unknown factors such as the idiopathic growth postponement syndrome. In this type of growth retardation, skeletal age, and height are often delayed to nearly similar degree. With medical treatment, however, it might be possible to achieve normal adult height.

It is difficult to differentiate between the two groups of growth deficiencies in those cases where bone age is postponed to a lower level when compared to the growth in height. Nevertheless, it is possible to differentiate primary and secondary growth failure by determining bone growth and bone age in the laboratory (Kaplan, 1990).

The height of children, who grow up under normal lifestyle conditions, is very much influenced by heredity. Hence, the final height of children could be postulated from the heights of parents. Different techniques for height estimations, which consider parental height, have been proposed (Rosenfeld & Cohen, 2002).

Gilsanz and Ratib (2005) stated that a child's height could also be estimated from the heights at an early age, with correlation in the order of 0.8. Although, young children are different mainly in the rate of development, some of them exhibit evident growth at quite on early age, whilst some have slower rate of growth, and finish skeletal growth quite late. Therefore, having skills in monitoring the rate of development will contribute to higher accuracy in estimation of height. A good way to acquire this skill is to make assessment of bone age, based on the hand-wrist image. The tables for estimation of final height based on height, bone age, age, sex and growth rate of bone have been published. Figure 4.1 shows the formula for the estimation of adult height proposed by Tanner et al. (1975):

Predicted Final Height = Height Coefficient × Present Height (cm) + Age Coefficient × Chronological Age (years) + Bone Age Coefficient × Bone Age (years) +Constant

Figure 4.1: Formula for the estimation of adult height

For females, researchers have also used the time of menarche to enhance accuracy in their estimations of bone age. The tables of coefficients for estimation of adult height for boys and girls are presented in Appendix D.

Another issue regarding the status of bone age assessment in UMMC is time taken to evaluate each X-ray image. King (1994) estimated the time for conducting BAA using the Greulich and Pyle method is 1.4 minutes. However, the result from observational study shows that the average time needed to assess the bone age, using a normal sample is 5 to 10 minutes. In the analysis of the data, 55.5% of respondents said they took from 5 to 10 minutes, 41.7% said that they spent from 10 to 15 minutes and 2.8% of respondents said they took from 15 to 20 minutes, to assess bone age using images of acceptable quality. Based on the result, it can be concluded that BAA is a time-consuming daily task in UMMC, especially, when a radiologist has to deal with many cases each day.

Table 4.6: Cases of BAA have to deal with in a week

Number of Cases for BAA	**Frequency**	**Percentage (%)**
About 5 to 10	28	78.9
About 10 to 20	8	21.9
About 20 to 30	0	0
More than 30	0	0
Total	36	100

Table 4.7: The Main reasons for conducting BAA

Main Reasons for BAA	**Ferequency**	**Percentage (%)**
Diagnosis of growth disorders	29	80.6
Estimation of height	4	11.1
Treatment of growth disorders using hormones	3	8.3
The patients without any document to indicate the age	0	0
Others	0	0
Total	36	100

Using the GP atlas for BAA has both advantages and disadvantages. The respondents replied to these questions differently. They were asked about the advantages and disadvantages of using the GP atlas as reported in the research by Garamendi et al., (2005). The respondents said that the GP method is easy to use, saves time, and is accurate. The disadvantages include it is time-consuming, has low accuracy, and the estimation is subjective.

From the feedback, 69.4% of the respondents said that it is easy to use the GP atlas and 22.2% said that produces accurate results, and only a few respondents (less than 10%) stated that it is time-consuming, or other reasons. The problems faced include: subjective estimation (52.8%), and time-consuming (36.1%). Furthermore, 8.3% of the respondents said that the GP method is not very accurate in estimation age for use in BAA.

The GP atlas has become the most popular standard for use in BAA. It contains two groups of normal radiographs of the hand-wrist of white girls and boys from upper middle-class families, who had participated in the Brush Foundation Growth Research from 1931 to 1942. When using the GP atlas, the image to be evaluated is compared to a large number of normal radiographs, and the age stated in the standard image that matches or most similar to images for evaluation, is the age of the children. Usually, it is quite easy to interpolate among the two standards to assign the correct age to the owner of an image. The obvious ease of use and also the speed, with which bone age could be determined, make the GP atlas the most popularly used standard of atlas for bone age assessment, in the world (Gilsanz & Ratib, 2005).

Table 4.8: Error Rate in BAA

Error rate	Frequency	Percentage (%)
From 3 to 6 months	7	19.4
From 6 to 12 months	11	30.6
From 1 to 2 years	13	36.1
From 2 to 3 years	3	8.3
From 3 to 4 years	2	5.6
More 4 years	0	0
Total	36	100

With regard to the normal error rate (estimation inaccuracy) of the current method, 36.1% of the respondents stated that the error rate is one to two years, 30.6% stated 6 to 12 months, 19.4% stated three to 6 months, 8.3% stated two to three years, and 5.6% stated two to three years (See Table 4.8). The difference in the error rates confirm that subjective estimation is the main problem in using the GP method. Thodberg et al. (2013) stated that human error resulting from low level of experience is the main reason of the low accuracy in manual method of bone age assessment.

4.2.3.4 Factors that affect bone age assessment

Although the assessment of bone age is dependent the on knowledge and experience of the people who assess the image, there are other factors which can affect the assessment. These include factors such as gender, race, socioeconomic situation, systemic illness, nutritional status, constitutional retardation, hypothyroidism, adrenal hypoplasia, etc., of the patients (Scanderbeg et al., 1998).

Gilsanz and Ratib (2005) expressed that some crucial caveats relating to skeletal age should be considered, for example, practical knowledge in bone age determination and similar analytic techniques are important to improve inter- and intra-observation.

Medical researches on skeletal age assessment have benefited from the involvement of skilled radiologists who use the same methods in bone age estimation. The standard rate of skeletal development is different between women and men, and also among people of different races. These references are definitely not appropriate for use in children with skeletal abnormality, endocrine dysplasias or a variety of other causes of growth retardation.

In this section, the respondents were asked to give their opinion on the factors such as race and gender of the patients, and noisy images, on the assessment of bone age. Table 4.9 shows the results of the analysis of the feedback from respondents.

Table 4.9: Factors Affecting BAA

Affecting Factor	**Race**		**Gender**		**Noise**	
	Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)
Yes	19	52.8	32	88.9	29	80.6
No	17	47.2	4	11.1	7	19.4
Total	36	100	36	100	36	100

Race or ethnicity is generally used in the context of genealogical relationships. Cavalli et al. (1994) divided race in to four main categories - African, Caucasians, Mongoloids, and

Australians. In this survey, 52.8% of the respondents said that race or ethnicity of patients could affect the assessment of the bone age.

Many researchers also investigated the different effects of gender on chronological age and skeletal age. Generally, the male skeleton is larger than the female skeleton. To make better comparison, the difference in the size and the weight must be considered within the context of ethnical classification, for example, Asian male skeleton versus Asian female skeleton. The difference in the skeletons of men and women is due to the effect of hormones on bone growth. Testosterone is the basic hormone that affects bone growth in men, whereas estrogen is the main hormone that influences bone growth in women. The maximum level of estrogen is at the age of puberty in the females. At age 18 years, the female skeletal bones are firm, while in the male, the bones are only set at age 21 years (Callewaert et al., 2010).

A basic distinction between the skeleton of a man and a woman could be seen in the limbs. In the male skeleton, the ulna, radius and humerus are the main bones of the hand and these bones are bigger than the same bones in the females. The bones of the fingers in men are also thicker and longer, that is why the men have bigger hands when compared to the women. The difference in size is also seen in the lower limbs that include the femur, fibula and tibia bones. Another main difference between the men and the women skeleton is the size of the pelvis bone. The pelvis in women is smaller and wider in shape than in men. The last bone in spinal column, called the tailbone, is more movable in women. The sacrum which is the end-point of the spine that connects to the pelvis is flatter in the women's body. These differences help in the process of childbirth in the females (Bruzek, 2002).

Analysis of the data shows that 88.9% of respondents confirmed that gender of the patient can affect the assessment of bone age, whereas about 11% of the respondents said that gender does not affect the estimation of skeletal age.

The respondents were asked for their feedback on another factor that can affect the evaluation of X-ray radiographs - noise on the images. Abbey and Barrett (2001) found that noise for brightness of images to be uniform, unless it changes the form of the images. There are factors, however, which are likely to cause variations in the quality of images, even when no details of the image are shown. This variation is random with no specific model. Usually, noise reduces the quality of images and makes them difficult to read.

All medical radiographs include some noises. The amount of noise causes a radiograph to become textured, grainy, and to have a snowy appearance. Noise of images can be introduced from variety of resources, and in fact, most imaging methods generate the noise, itself. Noise generally reduces the visibility of images and this is even worse in low contrast images.

Table 4.9 shows that 80.6% of respondents confirmed that noise in images could be a factor that can affect the assessment of bone age from radiographs. This finding is similar to findings by Abbey and Barrett (2001).

4.2.3.5 Alternative selection

Warren et al. (2000) stated that BAA is mostly carried out in the clinical environment and in forensic centres. It is obvious that these centres handle many of such cases, daily. The respondents were asked for their feedback about dealing with hand images of low quality or with incomplete images. Based on the feedback, 47.3% of respondents confirmed that they handle such images in their daily works. The respondents were also asked whether they have problem in using images of low quality. Based on the feedback, 69.4% of respondents said they have encountered problems, while 30.6% said they did not encountered problems. This shows that radiologists face difficulties in assessing bone age using incomplete images or very noisy images.

Time is an important factor in bone age assessment especially in the clinics, as mentioned in Section 4.2.3.3. Table 4.10 indicates the length of time which the respondents need to assess bone age using noisy images. It is not surprising that the results are different from the results mentioned in Section 4.2.3.3. The majority of respondents (47%) need from 10 to 20 minutes for evaluation of noisy images. Most of the respondents (55.5%) said they took from 5 to 10 minutes to assess bone age in normal image as mentioned section 4.2.3.3 whereas 38.9% said they took from 5 to 10 minutes to handle noisy images. On respondent (2.8%) said that he took more than 30 minutes to evaluate noisy images, and 11% of respondents said they took from 20 to 30 minutes.

Therefore, it can be concluded that noise in the image causes more time to evaluate the X-ray images because of the poorer visibility of the images (Abbey & Barrett, 2001).

Table 4.10: Time taken to assess noisy images

Time to assess noisy images	Frequency	Percentage (%)	Time to assess for normal images	
			Frequency	Percentage (%)
5 to 10 minutes	14	38.9	20	55.5
10 to 20 minutes	17	47.2	15	41.7
20 to 30 minutes	4	11.1	1	2.8
More than 30 minutes	1	2.8	0	0
Total	36	100	36	100

The respondents were also asked on the alternative BAA methods that can be used to deal with noisy images or incomplete images of the hand. A majority of respondents (72.2%) said they do not use alternative methods, while 27.8% said that do. They latter were further asked to specify the alternative method that they used for bone age assessment. A majority of them (70%), choose the knee bone, followed by the clavicle, elbow, and foot at the same rate (10%).

As mentioned in Chapter 2, Groupon Forensic Age Diagnostics, Germany, recommended that it would be more accurate to estimate of bone age is achieved if the experts used the combined evidence of growth from different bones. There are a number of reference atlases that are available for assessment of bone age based on other bones such as the elbow, foot-ankle, knee, pelvis, clavicle, etc. This study uses the clavicle bone to develop a combined system for BAA because the clavicle bone is considered to be a robust bone among members of the forensic science community. The clavicle is long bone that is used in both forensic practices and in archaeological anthropology because it survives burial even after a long time and it is an effective aging bone for studying bone growth in young adults (Singh & Chavali, 2011).

4.2.3.6 Significance and motivational factors for developing an automated BAA system

The last section in the survey questionnaire inquired about the significance and the factors that motivated the designing, developing, and implementation of an automated system for bone age assessment. With the advent of digital imaging, a number of researchers had tried to introduce computer-based systems for assessment of bone age. They have also used image processing methods to establish various reference databases of hand-wrist images of normal children to be used as benchmarks to automatically estimate the age (Pietkaet al., 2001). In order to overcome the difficulties of the manual approaches in BAA, the automated systems which have been developed are based on measurement of some ossification centres like the carpal or epiphyseal bones.

The questions in this section are aimed at finding out what radiologists expect from an automated BAA system that will replace the current manual methods. There were six questions in this section, and only answers with a mean value above 4 were considered. The respondents answered the questions by using a 5-point Likert-type scale ranging from (1 = Strongly Disagree, to 5= Strongly Agree). The responses, based on the highest mean value, are shown in Table 4.11. Each sub-factor is explained as follows.

Table 4.11: Motivational factors for developing an automated BAA system

Motivational factors	**Mean Value**	**Standard Deviation**
Do you agree to have a computerized system for BAA in UMMC?	4.31	0.710
An automated system would help the radiologist to speed up the process of BAA.	4.42	0.554
An automated system would increase the accuracy of the assessment of bone age.	4.17	0.775
An automated system in BAA would help to eliminate the observation variability.	4.36	0.593
An automated system based on the combined method using hand and clavicle bone should be able to solve the problem of noisy images.	3.86	0.683
An automated system to record the patients' age is able to manage the information more efficiently and effectively for further reference.	4.33	0.632

(A) Sub-factor One: Do you agree to have a computerized system for BAA in UMMC?

The Department of Biomedical Imaging in UMMC is considered to be one of the most important departments that deals directly with bone age assessment. Hence, it would expect that an automated system for BAA be implemented would be more reliable, faster, and give more accurate results. It is very time-consuming for doctors to prepare reports on BAA for diagnosis of growth disorders of patients or to monitor hormone treatment in growth disorders (Poznanski et al., 1978). When the number of problems increases, the use of automated methods would be able to cope with the estimation better, and more reliable results.

Therefore, an automated method for BAA that can save the time and energy would be welcomed by the doctors. The high mean value of 4.31 (out of 5.00) for the first statement shows that an automated system for BAA is a highly desired facility among radiologists in UMMC.

(B) Sub-factor Two: An automated system would help the radiologist to speed up the process of BAA.

One of the main factors in bone age assessment is time, which is a crucial factor in the clinical environment. From the results shown Table 4.10, it takes about 5 to 10 minutes to assess normal images, and about 10 to 15 minutes to assess noisy images to estimate the bone age of patients. It is obvious that respondents expect an automated system to speed up the process of bone age assessment. They have ranked this factor as the most important feature to have, as indicated by the score of 4.42, with standard deviation of 0.554

(C) Sub-factor Three: An automated system would increase the accuracy of the assessment of bone age.

Accuracy is of the most important factors in the age estimation process, hence, the pressing need to introduce an automated method for BAA in 1989 (Pietka, 1995). Accuracy is measured in terms of the difference between the age estimated by the system and the chronological age of patient. Accuracy is often synonymous with validity or trueness in BAA systems and is expressed with a standard deviation. The main objective for the development of different methods for BAA over the years has been in improving the accuracy and preciseness of the age estimation (Jong et al., 2007).

Hence, it is not surprising that respondents had express their desire to have a BAA system that can increase the accuracy in age estimation. The respondents have ranked this feature to be one of the important features to have in a BAA system. This is indicated by the score of 4.17, with a standard deviation of 0.775.

(D) Sub-factor Four: An automated system in BAA would help to eliminate the observation variability.

Table 4.8 shows that the difference in the error rates in assessment among the respondents ranges from three months to four years. This shows that the use of the manual methods in BAA produces the results which vary widely. One solution to this problem is to eliminate the variability in the observation in the manual method, by applying independent observer for all assessments of bone age. Buckler (1983) in his survey in the UK, found that about two-thirds of bone age assessment had been done by only an individual or three people in an organization. There have been reports in the literature about the observation variability caused by the use of various manual methods of bone age assessment, but which have been used as scientific evidences. Graham (1972) summarized the situation by stating “valid skeletal age assessment presupposes a working knowledge of the fundamental concepts and tools involved, and an amateur interpretation is often worse than none at all.”

Determination of bone age using an automated system eliminates the need to have people involved, and therefore, eliminates the subjectivity of the estimation. The elimination of observations variability is the second important feature to have in an automated system for BAA. The respondents gave it a score of 4.36.

(E) Sub-factor Five: An automated system based on the combined method using hand and clavicle bone images should be able to overcome the problem of noisy hand images.

To develop a good information system (IS), it is necessary to take into consideration the end-uses' needs, identify the main problems to be resolved so that good development plans can be formulated. The implementation a BAA system using the hand and the clavicle bones could address the missing data or noisy image problem in an automated system. Hence, the implementation of a BAA system based on the combined approach can overcome the problems of conducting bone age assessment on patients with hand injuries.

However, this factor has a mean value score of 3.86, based on the feedback from five respondents. This is considered an important factor or feature for overcoming the problem of noisy images or missing data.

(F) Sub-factor Six: An automated system that can record the patients' age is able to manage the information more efficiently, and more effectively, for future reference.

The need to introduce an automated BAA system to replace the current manual method is to solve the problem of redundant work. The automated system should have a large database containing information of patients for future references. The system will be a waste if it is unable to keep the record for the next report. The automated BAA system should produce accurate estimate of bone age, and should also store the information more effectively to satisfy the end-user's needs. This feature was given a score of 4.33.

4.2.4 Limitations

This is an exploratory research conducted using a questionnaire to obtain feedback on bone age assessment in the Faculty of Medicine, University of Malaya. In addition, analysis of the data gathered shows that 13.9% of the respondents stated that they had less than one year experience in BAA. The limitations of this survey are as follows:

i. The collection of data in the survey was limited only to the Faculty of Medicine, University of Malaya, specifically, the Department of Biomedical Imagining. The results from bone age assessment (BAA) procedure can be used in forensic centres, and in the criminal courts. There is an increasing demand to conduct BAA in the police and criminal investigation departments.

ii. Because of the restriction in collecting data from medical institutions or centres, the targeted respondents were from UMMC, only. Therefore, the findings cannot be generalized to include other medical centres in Kuala Lumpur, or elsewhere in the country.

iii. Systematic sampling might introduce biasness in the results.

4.2.5 Summary of survey

The survey participants are the radiologists from the Faculty of Medicine, University of Malaya. The printed questionnaires were distributed to the target respondents over two weeks. A methodical sampling approach was adopted. There were 36 returned questionnaires from the 55 questionnaires distributed, giving a response rate of 72%.

The survey was aimed at gathering data to have a better understanding of the status of BAA and to answer the research questions stated in Chapter 1. The survey findings address to achieve the first objective in the study and provided the answers to research questions 1 and 2.

Research Question 1:

What variability should be considered in the development of a computerized system for bone age assessment?

The research was aimed at identifying the variables and factors that can affect bone age assessment, from the medical perspectives. The targeted respondents were radiologists who conduct BAA as part of their daily task at UMMC. Table 4.9 indicates that 88.9% of respondents said that gender is one the variables that can affect the result in BAA, 80.6% said that noise in images, and 52.8% said that the race of patients are the other variables. Hence, the effect of these variables should be considered in the implementation a computerized system for BAA in order to obtain more accurate results of bone age.

Research Question 2:

What are the factors that can contribute positively to automated assessment of bone age in the clinical environment?

The findings from the survey indicate that BAA is routine task in UMMC, and about 79.8% of respondents conduct bone age assessment at least 5 to 10 times in a week. In the assessment of normal images, 55.5% of respondents said they spent an average of 5 minutes to 10 minutes, while 47% of respondents took 10 to 20 minutes to assess noisy images. On the question on how long it takes to become an expert in BAA, 33% said that it takes about 2 to 6 months, while 52.8% of respondents said that subjective decision is the biggest problem of using the manual method in BAA. Considering the large number of cases for BAA and the problems faced in the use of the manual methods for conducting BAA, there is a pressing need to use the automated approaches. Hence, it is not surprising that the respondents answer to the question, “Do you agree to have a computerized system for BAA in UMMC?’ obtained a score of 4.31 out of 5.00 as shown in Table 4.11. Thus, it could be concluded that automated method for bone age assessment is highly desired by the radiologists in UMMC because of the problems they faced currently with the manual methods for bone age assessment.

Chapter 5 will present the answers to research question 3 by explaining the design and development of a new automated method for BAA. The answer to research question 4 will be discussed in Chapter 6.

4.3 Results of the interview

The interviews were conducted over two weeks in February 2013 in UMMC and involved selected doctors from the Faculty of Medicine. The aim of the interview was to obtain more in-depth information on bone age assessment in UMMC from the experts in the field, themselves. The questions for the interview are listed in Appendix C.

Nine questions were prepared for the interview, and they were divided into three sections. The first section includes brief information on BAA in UMMC. The questions in the second section inquire about alternative methods for BAA, and the questions in the last section inquire about the motivational factors for implement an automated BAA system, and the users’ requirements the system should meet. The feedback from the interviews is discussed in the following subsection.

4.3.1 Discussion of interview results

The respondents who were interviewed comprised six staff members from the Department of Biomedical Imaging and the Department of Orthopaedic Surgery. The feedback to interview was recorded and analysed. The following Tables 4.13, 4.14 and 4.15 summarize the answers of the interview.

4.3.1.1 Analysis of first section

The first section of the interview, three questions were posed to obtain feedback on the BAA method used by the doctors, the main challenges and problems encountered, and the error rate from the use of the method.

All respondents informed that they have been using the Greulich and Pyle atlas and the manual method for BAA (see Table 4.12). From the feedback, it is clear that the experts in UMMC also used the same method for BAA as the radiologists pursuing their postgraduate studies. .

Table 4.12 : The response to the first section of the interview questions

Questions / Respondents	Q1: Main method used for bone age assessment in UMMC	Q 2: The maximum and minimum error rate	Q3 3: Main problems
R1	Using Pyle Atlas	Cannot estimate the exact error rate	- Not very accurate - Problems in dealing with deformity syndromes in children
R2	Using Pyle Atlas	It depends on the expertise of the observers	- Time-consuming - Low accuracy
R3	Using Pyle Atlas	About +/- 1 year	- Subjective standard
R4	Using Pyle Atlas	Cannot give an exact value	- Not precise
R5	Using Pyle Atlas	It is variable based on the observers and the quality of the radiographs	- Not accurate - Time-consuming
R6	Using Pyle Atlas	It depends on the skills of the radiologist	- Subjective decision - Observer variability

In answering question two, three respondents (R2, R5, and R6) stated that the error is not clear as this depends on the views of the radiologist or observers. Even R1 and R4 did not mention anything about the error rate, while R3 estimated the error rate to be about one year. If we compare the error rate mentioned by the experts in UMMC with the error rate mentioned by the radiologists (shown in Table 4.8), it is clear that the results from the use of the manual method depend on the knowledge and the experience of the observer. Thodberg et al. (2013) had emphasized that certain factors affect the role of human and this can lead to lower accuracy in the manual methods for estimation of bone age.

From the feedback of the interview, the main problems of the current method for BAA in UMMC are:

- Not accurate;
- Time-consuming;
- Subjective decision; and
- Problem in dealing with deformity syndromes in children

Table 4.13 shows that low accuracy of the manual method is the most important problem in using the Greulich and Pyle atlas - feedback from respondents R1, R2, R3 and R5. The second problem is that the manual method is time-consuming - R2 and R5 mentioned about the problem in using the Pyle atlas because they have to go through the atlas to find the best match. Another problem with the manual BAA method is the subjective decision - feedback from R3 and R5. The first edition of the GP atlas was introduced in the 1950s, and included the hand bones of Caucasians in the 1930s (Levick et al., 1986). The Pyle atlas only includes sample images of bones from normal people without any abnormalities or genetic disorders as mentioned in Chapter 2. Hence, the atlas cannot be used for assessment of bone age in children with deformity of the bone - feedback from R1.

4.3.1.2 Analysis of second section

Table 4.13: The response to the second section of the interview questions

Questions / Respondents	Q4 : Alternative method for bone age assessment in UMMC	Q 5: Selection of the second choice
R1	No suggestion to use other methods	Maybe elbow bone will be useful
R2	Do not have any idea	Not sure about the second choice
R3	Do not have any suggestion	No comments
R4	Do not have specific idea	Pelvic bone
R5	Do not have any idea	No suggestion
R6	No solution	No suggestion

One of the important problems when using GP atlas in BAA, as mentioned in the previous section, is determining bone age of children with bone deformity syndrome. As mentioned in Chapter 2, Groupon Forensic Age Diagnostics in Germany recommended that bone age assessment could be implemented based on combination of evidences for more assuring results, for example, using the left hand in combination with teeth examination or physical examination (Section 2.8).

However, all respondents had difficulties in answering Question four and Question five (Refer Table 4.13). The questions asked for suggestion for an alternative method for BAA, aside from using the left hand-wrist bones. This question looks for an accurate BAA method for children who have growth abnormality in their hand bones. As already mentioned, the Pyle atlas contains images of bones of normal healthy children, hence, it would not be a suitable source of reference for all people. Most of the respondents do not have any experience in using other bones in BAA except the hand bone. Hence, only respondent R1 suggested using the elbow because in case of fracture of the hand bones, the elbow can be used to estimate bone age. Respondent R4 suggested using the Pelvic bone as an alternative approach of children who have abnormalities in their hand, although he was not sure about the process and the method to use. The rest of the respondents did not have any experience in using other bones, and had no suggestion for an alternative method to use.

The results obtained for this section is similar to that mentioned in section 4.2.3.4 on feedback from radiologists for suggestion of an alternative approach for handling noisy images. Only 27.8% of respondents have an alternative suggestion to deal with noisy images or missing data. The majority of respondents, however, chose the knee and only 10% suggested using the elbow and the pelvic bones.

Table 4.14: The response to the third section of the interview questions

Questions / Respondents	Q 6 : Importance of automated system for BAA in UMMC	Q 7: Prefer the manual method or automated method	Q 8: Features of computerized system	Q9: web-based system or stand-alone system
R1	Should be useful	Automated	-High accuracy - Easy to use	web-based
R2	An interesting area for research	Automated	-Reliable - Faster than human	web-based
R3	Agree with automated system for BAA	Automated	- Accuracy	web-based
R4	Useful and effective	Automated	- Speed - Accuracy	web-based
R5	Interested to use an automated system	Automated	- Accuracy - Effectiveness	web-based
R6	Agree with automated system for BAA	Automated	- Time - Accuracy	web-based

4.3.1.3 Analysis of third section

In replying the last four questions in third section, the respondents seemed to have similar ideas for questions six, seven, eight and nine (Refer Table 4.14). Based on the finding above it can be concluded that:

- All respondents agreed on the importance of having an automated system for BAA in UMMC. They said that the computer-based system is more useful than the manual method;
- The respondents prefer the automated method for BAA;
- The most important features of the computerized system for bone age assessment are accuracy, speed, efficiency, and ease of use;
- The web-bases system is preferred over the stand-based system.

In this subsection, respondents are asked to suggest the requirements of a computerized system for BAA. Their suggestions could be useful for the researcher to identify the end-user' requirements from the experts' perspective, for designing, developing, and implementing an automated BAA system.

4.3.2 Summary of interview

A structured interview, based on the approach proposed by Berst et al., (2001) was conducted with six doctors from the Faculty of Medicine, University of Malaya. The interview respondents were specialists from the Department of Biomedical Imaging and the Department of Orthopaedic Surgery. The nine interview questions are divided to three parts. The interview is aimed at getting an overview of the status of BAA in UMMC, and identifying the requirements, based on the experts' perspective for developing an automated system. An analysis of the feedback of the interview provides a better understanding of the problems that doctors face while using the GP atlas for bone age assessment in UMMC.

The feedback to the interview indicates that experienced medical specialists are more inclined to recommend using an automated method to replace the manual method for BAA. All respondents agreed on the significance of a computerized system for BAA to eliminate making subjective decision and to reduce the time spent on estimation of bone age. The majority of the respondents emphasized that it is important for an automated BAA system to be more accurate and be more effective in estimation of bone age. In addition, an automated BAA system would reduce the time spent on BAA and increase the reliability of the final decision.

Therefore, the outcome from this study would not only assist the radiologists (people who deal with bone age assessment) but also medical experts or specialists to obtain more accurate results and speed up the BAA process.

4.4 Results of Observational Study

The place of the observational study was an X-ray lab in the Department of Biomedical Imaging. The goal of the observational study is to obtain a full understanding of the radiologist's behaviour and how they carry out bone age assessment. All data and responses from observation were recorded and analyzed. The qualitative analysis was done based on the results and the answers to the questions. Table 4.15 shows the answers to the questions.

Table 4.15: Answer to questions in observational study

No.	Question	Response
1	Background Information of respondent	- 30 years old - Master's level student - 3 years of experience in bone age assessment procedure
2	Using BAA technique in UMMC	- Training starts in first semester of postgraduate course
3	Common method for BAA	- Hand-wrist bone - The GP atlas - The TW atlas
4	Reasons for doing BAA	- Monitoring or confirming bone growth in children - Examination of hormone blood doses - Diagnosis of precocious puberty - To make decision on treatment of growth disorder - Estimation of children's height
5	Identify the problems.	- Children with disorders of bone mineralization - Pathological problems - Absolute diagnostic marker - Different observers
6	Frequency in using BAA	- 10 to 15 cases, daily
7	Significance of BAA	- Deciding on whether there is retardation of growth Investigation the time of hypogonadism - Decision on growth hormone replacement therapy in children

The respondent was a postgraduate student in the Department of Biomedical Imaging. The observational study started with the sharing of some general information about the respondent to address the first part of study as follows:

- The respondent is a 30 years old local student.
- She is studying in the Master of Radiology programme and she is in the third semester in programme.
- She has three years experiences in bone age assessment, (this is one of the reasons for selecting her for this observational study).

Question two is used to probe into the background on training in BAA in UMMC. According to the respondent, the radiologists received training in bone age assessment when they are pursuing their Master's programme. It is a compulsory training that takes place from the first semester of the Master programme. The training is usually scheduled for three weeks at the beginning of each semester.

In answering the third question, the respondent informed that the most popular method used in UMMC for the assessment of bone age is the use of the hand-wrist bones, although there are some factors that could affect the bone age such as sex of the patient, systemic diseases or growth abnormalities. In addition, the Greulich-Pyle (GP) atlas is the most commonly used method for determining the bone age by the radiologists in UMMC. The respondent showed the researcher the PDF version of the second edition (1988) of the GP atlas that was installed in the computers in the X-ray labs. The file contains 63 pages of hand X-ray images from infants up to children of age 18 years. The original hardcopy version of the atlas was lost about eight years ago.

The Tanner and Whitehouse (TW) atlas is also used in UMMC. The TW atlas has less variability in the margin, and is more accurate, but it is more time-consuming, hence, the GP atlas is more widely used in UMMC.

Milner et al. (1986) stated that the GP atlas is the most common method used by radiologists for assessment of bone age because it is easier to use and takes less time to estimate bone age.

Based on the feedback from the respondent, the main reasons for applying BAA in UMMC are as follows:

- To confirm normal physical of growth or diagnose growth abnormalities in children. Examples of growth abnormalities include: familial short stature (FSS) that concerns abnormal skeletal growth or constitutional growth delay (CGD) that concerns delayed skeletal maturity;
- Examination of level of blood growth hormone doses in children during puberty. Such as conducting laboratory test on pituitary-gonadal axis in delay of puberty. It means that it cannot visit values of LH or FSH in children with bone age below 12 years;
- Examination of precocious puberty (rapid telarche or rapid puberty) and situations of hyper organisms like congenital adrenal hyperplasia (CAH) that can be identified by advanced skeletal age;
- For making decision to treat the patients with CAH or precocious puberty and to control the skeletal growth with GnRH analogs or hydrocortisone; and
- For estimation of children's height.

With regard to the last reason, the respondent explained the problems faced in UMMC. She said that using bone age assessment could be misleading because of various factors:

- Some children has disorders of bone mineralization;
- Some children have pathological problems;
- Bone age assessment is not an absolute diagnostic marker for height of children;
- Different observers might use different methods for investigating children's height.

In answering question six in the observational study concerning the frequency of using the BAA technique by radiologist in UMMC and the average time spent for assessment of bone age, the respondent said that during her normal working day, she handles around 10 to 15 cases.

The average time taken to assess the bone age, in a normal situation (where the radiographs are of normal quality) is 5 to 10 minutes. It can be concluded that a radiologist in UMMC spends about two hours of her/his time for bone age assessment of patients, daily.

The last part in observational study is to find out the significance of bone age assessment for a radiologist. The respondent said that estimation of bone age of patients is useful from various aspects, such as:

- Making decision about growth retardation and delayed or advanced puberty of children;
- For investigating the exact time on replacement hormone treatment of hypogonadism in children ; and
- Making decision on growth hormone replacement therapy in children.

4.4.1 Summary of observational study

From the observational study, we arrived at some conclusions regarding the application, significance and the challenges of assessment of bone age in UMMC. It is found that the doctors and radiologists used the bone age assessment for the evaluation of skeletal maturity to determine physical growth and even biological age. Bone age is an indicator for radiologists and doctors to determine puberty disorders in children. Although bone age can provide useful information about the children’s age, the information could be misleading if not properly used. Doctors used the hand-wrist X-ray image to estimate the bone age in UMMC. The two methods used for BAA involve the use of the GP and TW atlases. Although the TW method produces fewer errors, the GP method is used more frequently, because it is easier to use and is less time-consuming.

Based on the above observation on the behaviour of the radiologists involved in BAA, it is evident that analysis of bone age is important in treating patients. The study also reveals that specialists spend about two hours each day to assess bone age. Thus, the development of an automated system for bone age assessment can bring significant benefit in the clinical environment.

From the observational study, it can be concluded that an automated system to assess bone age on will be useful for the following reasons:

- It provides an accurate assessment of the actual age;
- It eliminates the variability in the estimation of bone age; and
- It reduces the work flow and the time needed to determine bone age.

The next sections discuss two other types of information gathering techniques that are used to solicit data for this research.

4.5 Conclusion

The study was carried out to verify the factors that can contribute to the success of implementing an automated system for bone age assessment. This is an exploratory study, hence, a questionnaires survey, interviews and an observational study were used for collection of data. The targeted respondents were radiologists and doctors from the Faculty of Medicine, University of Malaya. They are considered to be experienced and knowledgeable people in BAA. Based on the outcome of the questionnaire survey and interviews the first research objective has been successfully achieved. The next chapter will discuss the framework for an automated BAA system and the development process of the system.

Chapter 5: Design and Development of Bone Age Assessment System Using Images of the Hand and the Clavicle (BAASHC)

5.1 Introduction

This chapter discusses the design and implementation of the BAA system. The main contents of this chapter are derived from Chapter 2 and Chapter 4. In Chapter 2, we reviewed the existing bone age assessment (BAA) systems that will be used in the first level of the proposed system and the analysis of the survey results and feedback to the interviews in Chapter 4, were used to identify the factors that can affect BAA, as well as and the end-user requirements in an automated BAA system for medical application. The relationship between Chapter 2 and Chapter 4 and this chapter is illustrated in Figure 5.1. This chapter explains the design and development of a bone age assessment system based on the use of images of the hand and clavicle bones based on the analysis, design, development, implementation and evaluation (ADDIE) model.

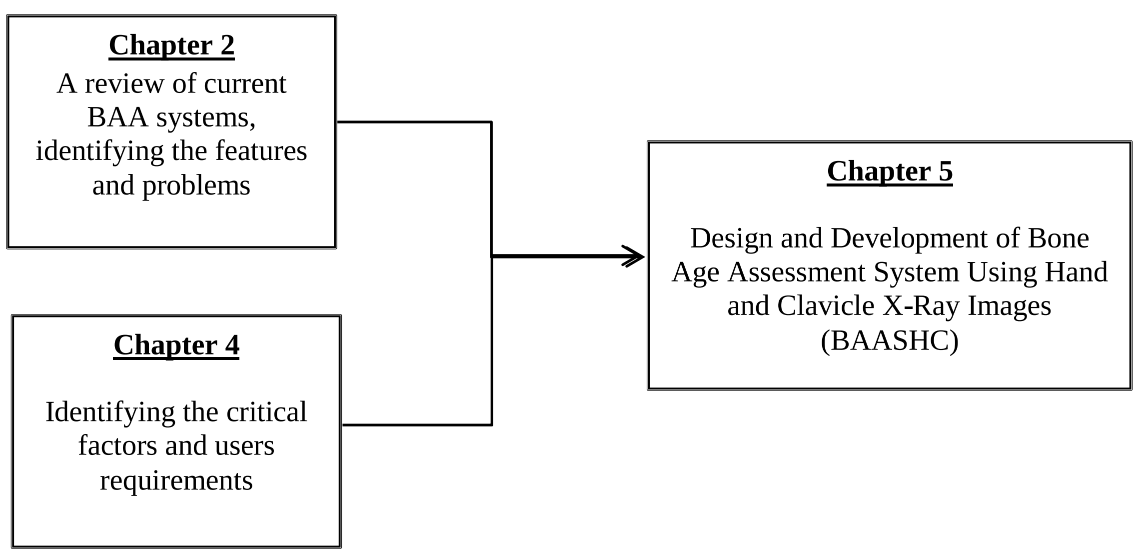

Figure 5.1: The relationship between Chapter 2 and Chapter 4 and Chapter 5

5.2 System development methodology

System development methodology is the process involved in planning, designing, and implementing an information system. This research uses the Analysis, Design, Development, Implementation and Evaluation (ADDIE) model as its system development methodology.

The ADDIE model was developed by Florida State University for the processing of instructional systems development (ISD) approach for military services training. The ADDIE model is defined as an adjustment of the system engineering plan to solve the problems in the workplace of instruction (Peterson, 2003). This model uses the alternative solution for problem instructional which selection is based on the most effective results. The ADDIE model tries to save time and money by identifying problems while they are still easy to solve (Allen, 2006).

The ADDIE model involves five phases, as shown in figure 5.2. The next sections will discuss the five phases in details and explain how they are applied in this study.

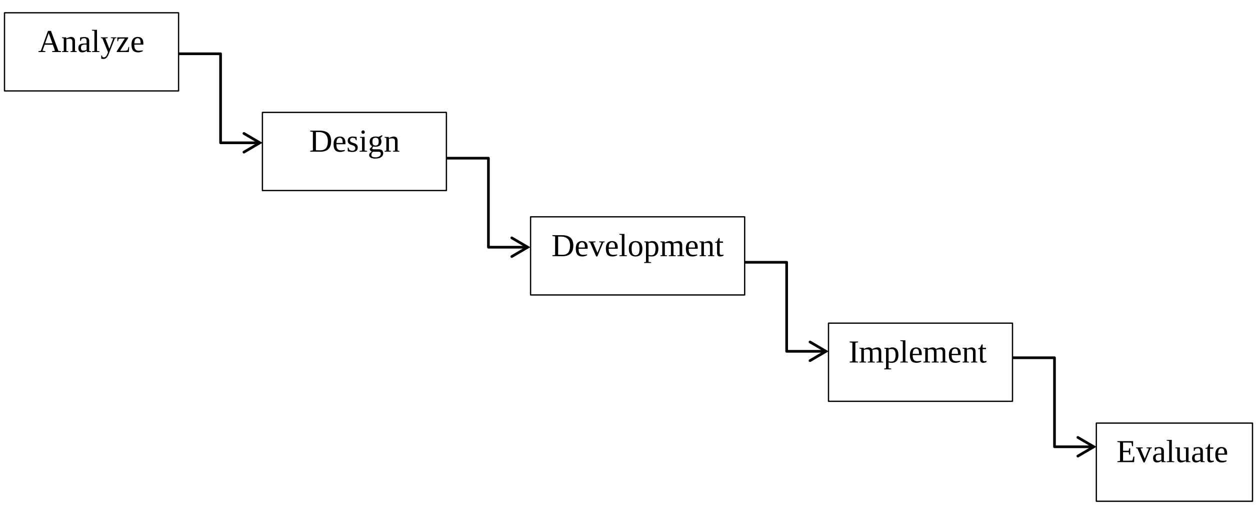

Figure 5.2: Five phases in the ADDIE model

5.2.1 Analyze phase

The Analysis phase is the most important phase in the ADDIE model. The analysis phase involves identification of the problems instructional as well as the objectives, and focuses on the environment, knowledge and skills. This level was discussed in Chapter 2 and Chapter 4. The review on automated methods for bone age assessment (BAA) in Chapter 2 highlighted the fundamental problems in image processing techniques and segmentation of the region of interest (ROI) in the hand images. Furthermore, it highlighted that the role of the other bones in young adults, as well as in handling forensic cases where defects and other abnormalities and injuries on the hand are presented in the current automated BAA system were ignored. This is the reason for developing a novel automated BAA system that uses a new image processing approach for the hand and clavicle X-ray images.

The study was carried out to identify the factors that can contribute to the success of developing an automated system for bone age assessment. Hence, a questionnaires survey and interviews were used for data collection.

The respondents were radiologists and specialists from the Faculty of Medicine, University of Malaya. They are considered to be experienced and knowledgeable people in BAA. Based on the outcome of the questionnaire survey and interviews the first research objective has been achieved. The questionnaire survey was aimed at identifying the variables and factors that can affect bone age assessment, from the perspectives of medical specialists. Table 4.9 shows that a high percentage of respondents said that gender, noise in images, and the races of patients are the variables that can affect the assessment of bone age. Hence, this system will consider the effect of these variables in the developments of the system to obtain more accurate results of bone age.

From the results of interviews it can be concluded that automated system for BAA is highly desired by the specialists in UMMC. The results of the interview provide a better understanding of the problems that doctors face while using the GP atlas for bone age assessment. All respondents agreed on the need to have an automated method for BAA to eliminate observational variability and to reduce the time spent on assessment of bone age. Furthermore, an automated approach for BAA would reduce the time spent and increase the reliability of the final estimation.

The basic target aim in this project is to produce a system that is capable for solving of BAA problems in both the hospital and forensic center, based on the user requirements. The user requirements are to serve as the mandate of reference for the design, development and implementation of a system. The goal of the user requirement is to provide a clear understanding of requirements as an early input to development system (Xie & Meng, 2011). The main requirements are identified from the data collection in Chapter 4 as they are listed in Table 5.1:

Table 5.1: Summary of user requirements from data collection

Data Collection Method	**User Requirements**
Survey Questionnaire	▪ Speed up the process of BAA ▪ Increase the accuracy of BAA ▪ Eliminate the observation variability ▪ Using hand and clavicle bone to solve the problem of incomplete or noisy images ▪ Consider the factors that affect BAA ▪ Record the age for further reference

Interview	▪ Use automated system for BAA ▪ Improve the accuracy in BAA ▪ Decrease the time in assessment ▪ Easy to use ▪ Have a web based application
Observational Study	▪ Using Hand images for BAA ▪ Improve the accuracy in assessment ▪ Remove the human observation

The findings of collected data address to achieve the requirements in the study and what radiologists and specialists expect from an automated BAA system that will replace the manual methods. Table 5.1 shows, it is expected that our automated system for BAA need to be faster, and assess more accurate results. It is time-consuming for radiologist and doctor to prepare the reports on BAA, hence they require in decreasing the time of BAA in the system. Furthermore, the system that can save the energy and eliminate the human observation would be preferred by the users. Assessment of bone age using a fully automated system removes the need to have people involved and it is eliminates the subjectivity of the estimation.

To design and develop a success information system (IS), it is necessary to identify and consider the end-user' requirements. Using hand and the clavicle bones could address the missing data or noisy images problem in our system. The implementation of a BAA system based on the hand and clavicle bones can overcome the problems of conducting BAA on patients with hand injuries.

The need to introduce an automated BAA system to replace the current manual method is to solve the problem of the repeated work. The BAA system should assess accurate results, and also should store the information more effectively to satisfy the end-user. The following sections explain how all the user requirements are applied in the designing, development and implementation of BAA system.

5.2.2 Design phase

The design phase is systematic and deals with assessment instruments, performance, exercises, content, lesson planning, and resources. In this phase the information gathered in the analysis phase is used in designing the system which meet the needs of end-users. Testing the concepts in the design phase will save time and money (Allen, 2006).

5.2.2.1 Principle of system design

Determination of bone age based on radiological evidences or X-ray images has an important role in forensic studies. Based on the feedback of data collection, generally this procedure is carried out manually based on comparison of the radiographs of the left hand–wrist bones, hence, it is time-consuming. This research is aimed at developing an automated system to assess bone age based on the radiographs of the hand and clavicle bones (BAASHC). This automated system will eliminate the variability of observer and increase the accuracy of age estimation. The proposed BAASHC consists of two main subsystems:

Subsystem BAA1: An automated system for detecting the age of people based on the hand-wrist X-ray images; and

Subsystem BAA2: An automated system for detecting the age of people based on the X-ray images of the clavicle bone in patients with abnormalities in their hands, for forensic purpose.

Figure 5.3 shows the general workflow of the proposed system for bone age assessment and its two subsystems.

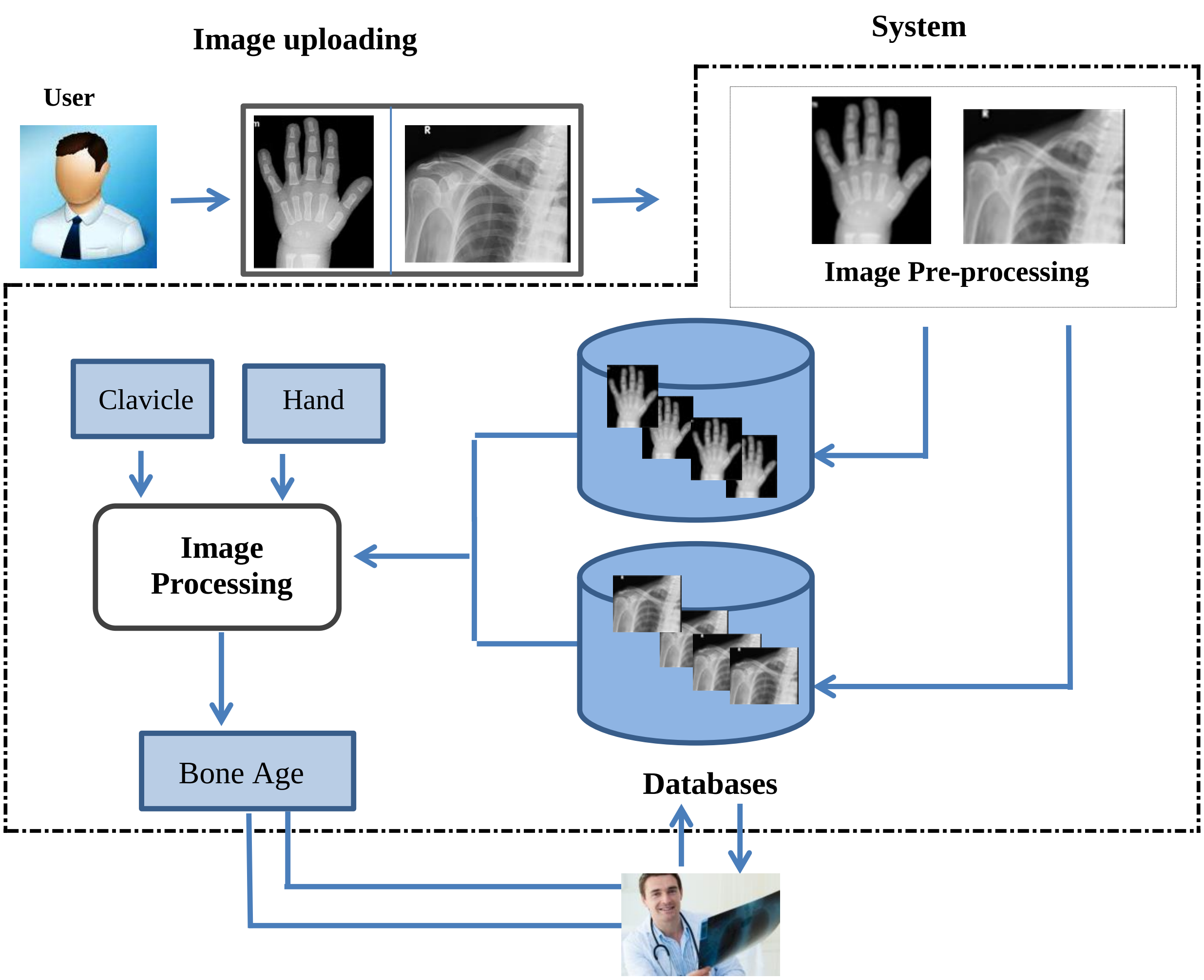

Figure 5.3: Framework of BAA system using hand and clavicle bones (BAASHC)

In order to have a better understanding of BAA in general, and BAASHC, the above framework is decomposed into four segments, as shown in Figure 5.4. Each segment is discussed in detail in the sections below.

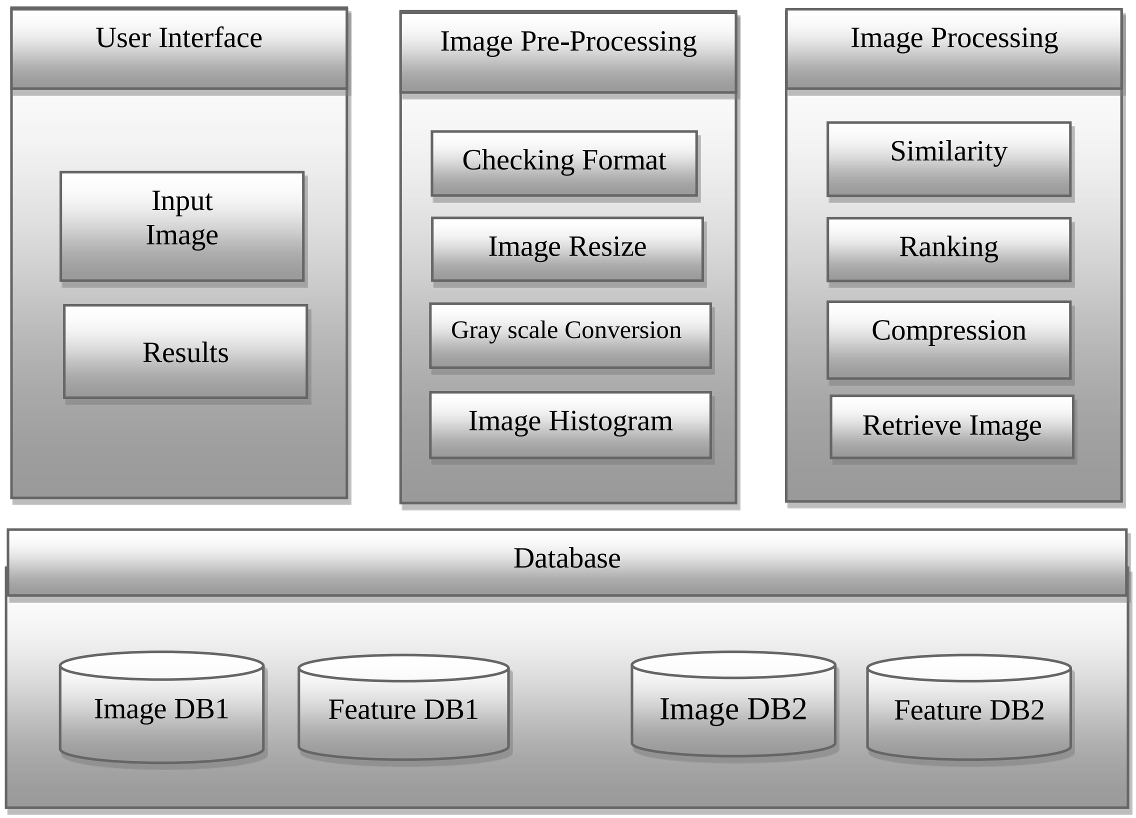

Figure 5.4: The different segments of the proposed system (BAASHC)

5.2.3 Development of BAASHC based on histogram

The development phase focuses on building on the outcome of the design phase. In the development phase, the developers and designers produce and assemble the content assets that had been blueprinted in the design stage.

The proposed system consists of four main segments as shown in Figure 5.4. The first segment: User Interface - connects the users to the system using a web-based Graphical User

Interface (GUI). The second segment: Image Pre-possessing converts an image into a grayscale image, resize the image, and generate the histogram of the image. The third segment: image processing - this is the main level in the process of estimation of bone age. It consists of four parts - Similarity; Ranking; Compression, and Retrieve Image. The final segment: - this is the database that contains different tables.

5.2.3.1 User interface

In this research, a web-based interface for BAASHC was set up and made publicly accessible. The web-based interface was developed based on the feedback to the interviews in which all doctors voiced their preference for a web-based BAA system. Muller et al. (2006) in their survey also found that doctors prefer to use web search engine and web-based interface for retrieving images from the archives.

PHP is a well-known programming language that has been used to develop interface for a MYSQL database with an Apache web server on a windows-based server. The graphical user interface (GUI) is segmented horizontally into separate parts - header, navigation bar, status bar, and different tabs - and shown as icons. The GUI makes it easy for users to switch between different parts of the interface. The graphical user interface is developed to give a visual guide to the system functions which could include uploading images and displaying the results.

The lack of a suitable graphical user interface (GUI) in the computerized systems of medical facilities such as the radiology department, is termed as the “application gap“ (Deserno et al., 2009). In this study, the web-based graphical interface user was developed for BAASHC in order to fill the application gap. The BAASHC system could easily be setup in the internal network of the hospital.

A user can upload a radiograph of a hand-wrist or a clavicle to the web server of BAASHC. After the pre-processing and processing phases have been completed, the system will output the estimated bone age. Only images in PNG format of the hand-wrist with size (333*512) pixels and size (666* 490) pixels of the clavicle are allowed to be uploaded into the system. Figures 5.5 - 5.8 illustrate four screenshots of the system. Figure 5.4 shows the index page, where the user can browse BAASHC using the internet browser.

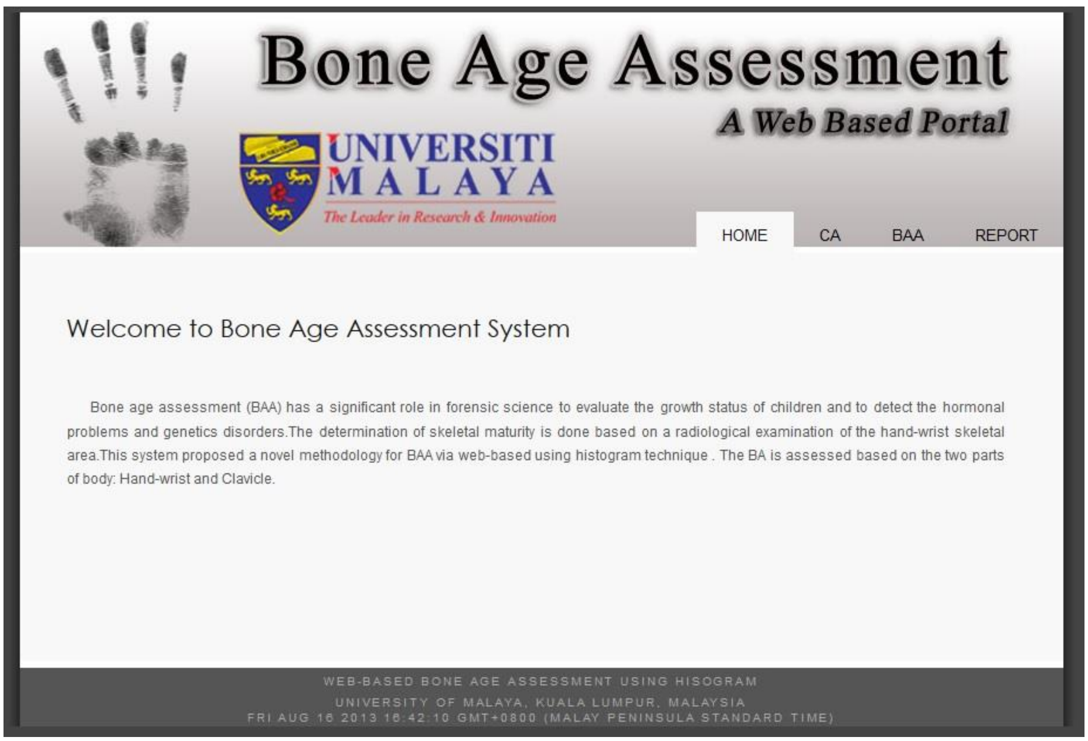

Figure 5.5 : A screen shot of homepage of BAASHC

There are four tabs in the top menu in the index page - Home, CA, BAA, and REPORT tabs. Figure 5.6 shows the main tab in the system. This page shows the three options for bone age assessment:

- Bone Age Assessment Based on the Hand Bones;
- Bone Age Assessment Based on the Clavicle; and
- Bone Age Assessment by Radiologist.

Figure 5.6: A screen shot of BAA page

Mackay (1952) stated that hand is the most suitable bone to be used for age estimation because the various bones in the hand-wrist change in parallel with the change in physical maturation. The results of the survey and interviews discussed in Chapter 4, also reveal that the doctors and radiologists in UMMC prefer the hand-wrist bone for conduction BAA.

In this research, a new method for BAA was developed based on the images of the hand and clavicle bones for BAA. This method helps to overcome the problems stated in Chapter 2 and Chapter 4 as follows:

- Noisy images of the hand which are not clear enough;
- Children with abnormalities in the bones of their hand; and

- Forensic cases seen with defects in the hand because of unexpected incidents or injury.

Groupon Forensic Age Diagnostics in Germany stated that combined evidences for bone age assessment produce more accurate results, especially, in forensic practice. However, there is still no robust method for age estimation using the combined method, reported in the literature. The clavicle has been selected in this system because this bone is one of the main bones used in forensic work or investigation. The clavicle, as a long bone in the body, survives after burial even for a long time due to its highly compact nature (Singh & Chavali, 2011).

In the proposed system, the user can choose to do bone age assessment using the hand or the clavicle, as shown in Figure 5.7 and Figure 5.8, respectively.

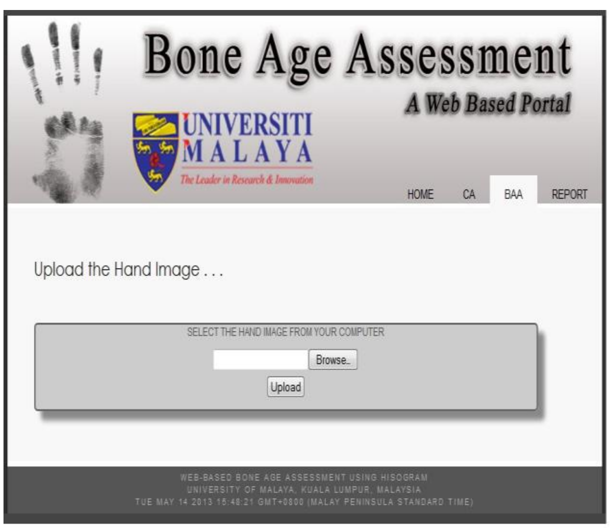

Figure 5.7: A screen shot of uploading the hand image in BAASHC

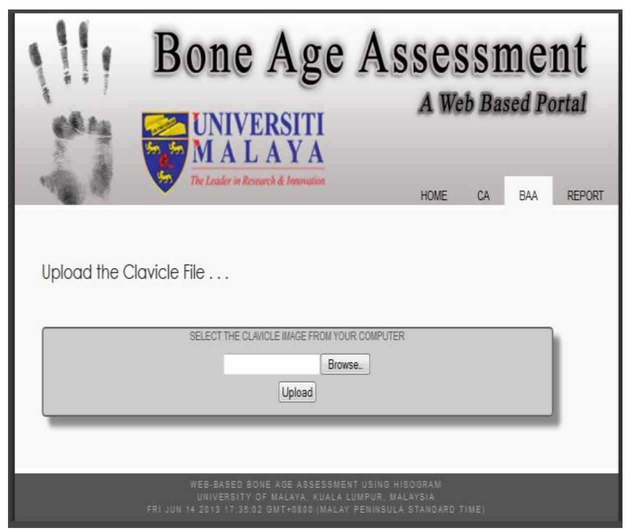

Figure 5.8: A screen shot of uploading the clavicle image in BAASHC

5.2.3.2 Image pre-processing

The process of bone age assessment starts with an X-ray image of the hand-wrist or a clavicle radiograph in digitized format. The radiograph in the PNG format is uploaded to the system by the user or a radiologist. The pre-processing stage consists of the various levels, and starts after the uploading of the image. The pre-processing stage prepares the images for subsequent process in bone age assessment.

The requirements of the pre-processing stage are based on the subsequent techniques used in the bone age assessment method (O'Keeffe, 2010). From the literature review, it is found that many of the automated BAA systems apply extraction of region of interest (ROI) as part of the preprocessing stage for segmenting the images for further analysis. For example, the preprocessing method in the system developed by Hsieh et al. (2007) included techniques of thresholding and heuristic searches thresholding. A phalangeal region as ROI was selected by scanning the area and fixing the angle. The output of preprocessing stage in this system is the extraction of phalangeal bones together with the Gabor filters for smoothing the edge. This stage prepared the system for bone segmentation in at the higher levels. The thresholding method and knowledge-based search method are the most well-known techniques used for ROI extraction in the majority of computerized BAA system. These techniques produce the soft tissue of the hand bone and extract the fingers or radius or ulna bones. They used the systems developed by Michael and Nelson (1989), Pietka (1991), Luis-Garc et al. (2003), Zhang et al. (2006), Hsieh et al. (2007) and Thodberg (2009) for identifying the regions of interest.

The preprocessing stage enhances the robustness and preciseness of the image processing based on computerized analysis (Pietka et al., 2001). The preprocessing stage involves the initial screening of the hand and clavicle X-ray images. This level plays a very important role in standardizing the radiographs, because the original images include some irregularities. Although there is no possibility of managing all variations of the radiograph features in this system, the main objective is in developing an automated technique for bone age estimation, and attention is given to the role of the combined method in BAA. A number of assumptions have been made in order to concentrate on the main objectives of this study:

- The uploaded X-ray images include the left hand-wrist or the clavicle;
- The uploaded X-ray images is in the right direction;
- All bones in the radiographs are clearly visible; and
- The X-ray images are of reasonable quality for analysis by a radiologist.

The outputs of the preprocessing task are used for the main processing stage for estimation of bone age. The proposed preprocessing stage for this system involves four main steps:

- Format checking;
- Gray scale conversion ;
- Image resizing; and
- Image histogram.

- **Format Checking**

In the first stage of the preprocessing task, the format of the uploaded images is checked. As mentioned in the previous section, only the PNG format (PNG is a define standard) is accepted for uploading to the system. If the users try to upload images in another format, by mistake, the system alerts the user about this. Figure 5.9 shows the program codes used for format checking in the file upload page:

```
if (($_FILES["file"]["type"] == "image/png")))
 {
  if (file_exists("temp/" . $_FILES["file"]["name"]))
   {
   }
  else
   {            $genUFN=uniqueFileNameGen();
                $newname=$genUFN.".png";
   move_uploaded_file($_FILES["file"]["tmp_name"],
   "temp/".$newname);
   $fileLoc="temp/".$newname;
        $_SESSION['tmp_filename']=$fileLoc;
        $_SESSION['tmp_fileID']=$genUFN;
        echo "<b>Your File ID ".$genUFN."</b>";
   }
 }else
 { echo "Invalid file"; }
```


Figure 5.9: The code for format checking in the file upload page

Figure 5.10 illustrates a screenshot of the format checking stage when the user mistakenly uploads a JPEG file and the system error message which is displayed.

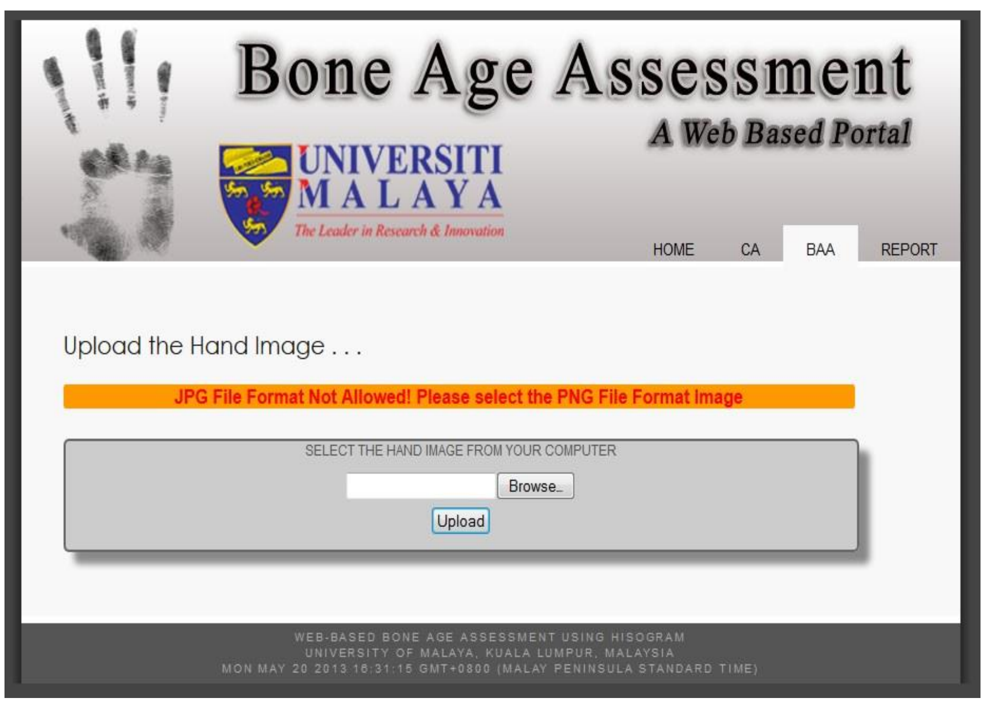

Figure 5.10: Alert message in image file format checking stage

- **Image Resizing**

The sizes of uploaded images are computed by cropping the border to the size of (333*512) pixels for hand images, and (666*490) pixels for clavicle images. If the size of the uploaded images is between these two defined sizes, the images will be validated for further processing otherwise, the system will ask the user to crop the border. The class of imageCrop.PHP includes the functions for cropping. Figure 5.11 shows the system message when the size of the image does not conform to the pre-defined allowable size.

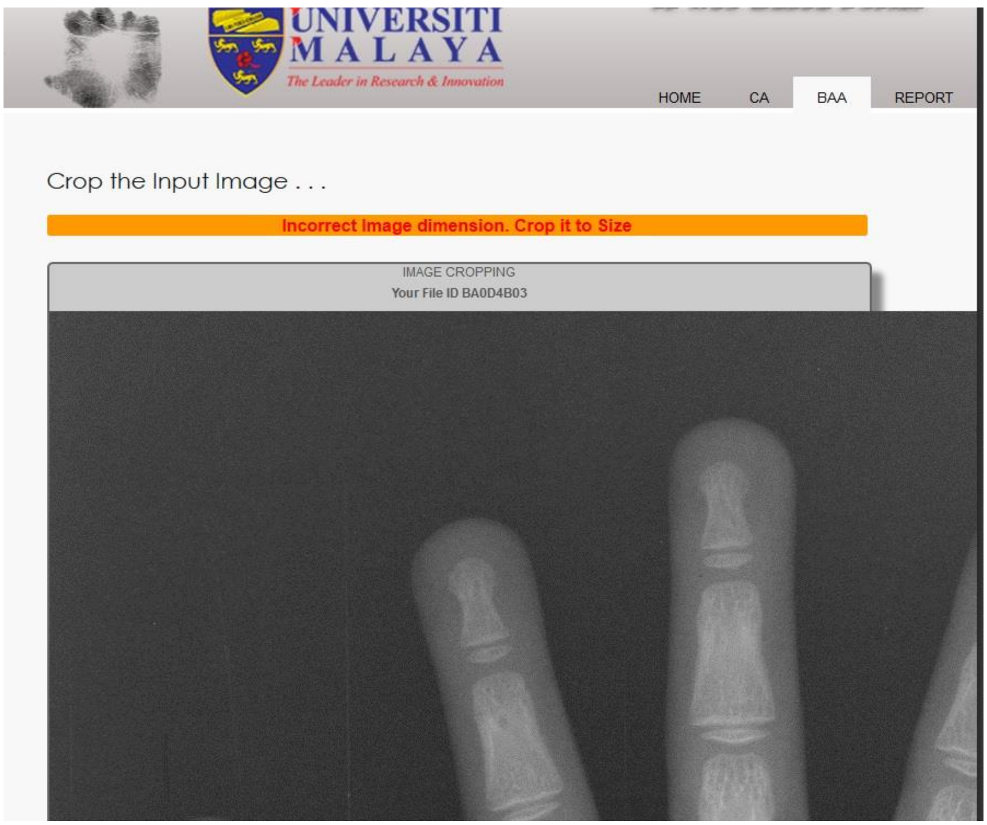

Figure 5.11: The alert message for cropping the image

Figures 5.12-513 show the image cropping process to conform to the predefined allowable size.

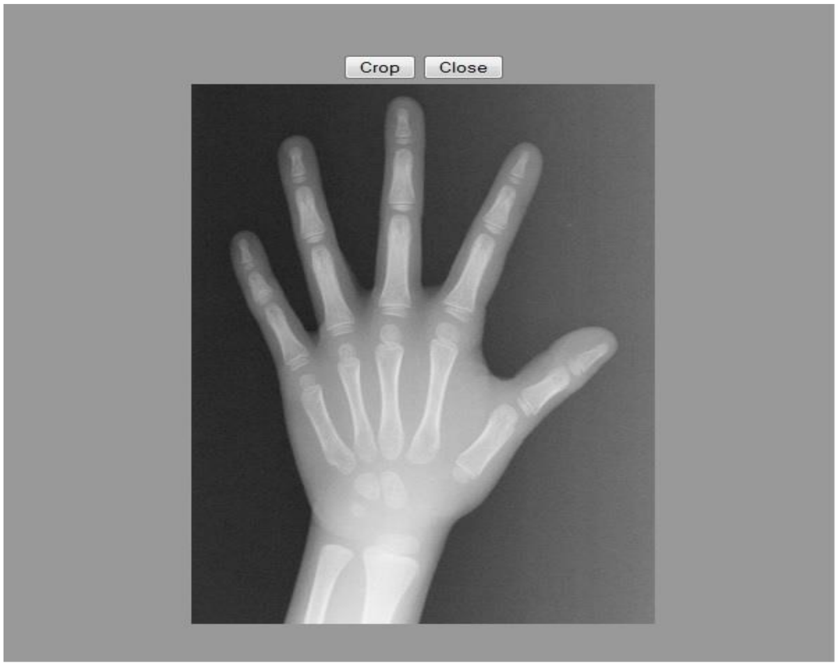

Figure 5.12: The cropping process

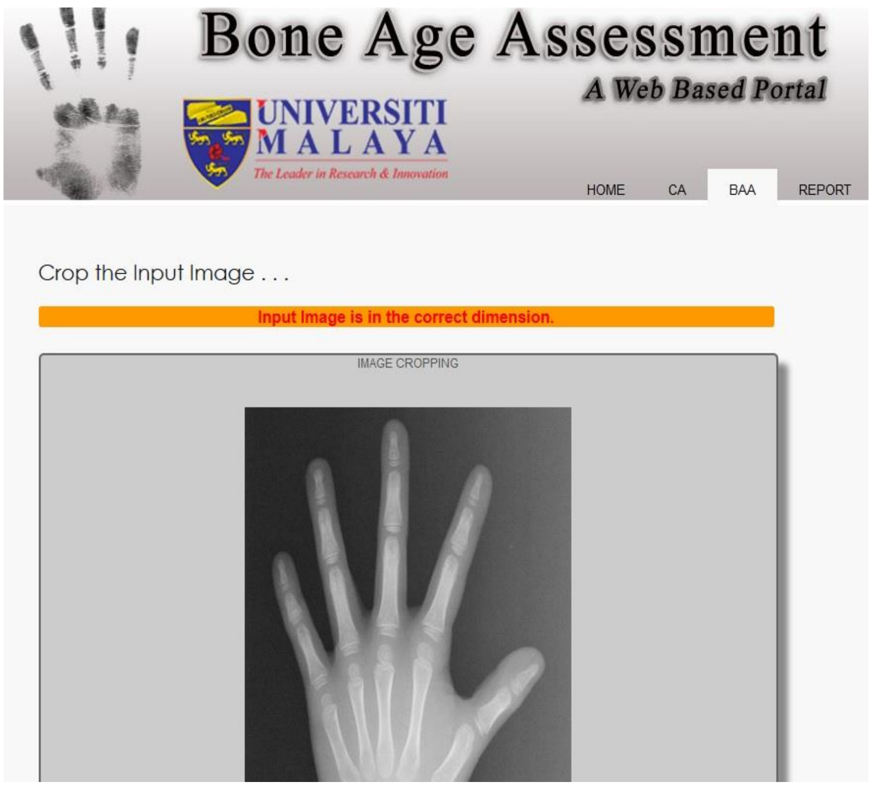

Figure 5.13: After cropping the image to the correct dimension

- **Gray Scale Conversion**

A gray scale image is very useful for processing the original image. In this step, the system automatically converts the cropped X-ray image from an RGB to gray scale format. Gray scale images have 256 hues of different intensities; hence, the generated histogram displays 256 counts of distributed pixels from the image's gray scale values. When our system converts the gray scale image into a binary image using thresholding, the histogram is used to decide the value of the threshold to be used. A bi-model histogram is used to determine if the image is suitable for thresholding. In addition, generally, all X-ray images are in gray scale format. Hence, gray scale image will give more accurate results compared to colored image.

A built-in function in PHP (see Figure 5.14) - the image filter - is used to convert the images into the gray scale version:

```
$image = imagecreatefrompng("ip7.png");
 imagefilter($image, IMG_FILTER_EDGEDETECT);
 imagefilter($image, IMG_FILTER_GAUSSIAN_BLUR);
 //imagefilter($image, IMG_FILTER_EMBOSS);
 imagepng($image,"ip7_e.png");
 imagedestroy($image);
```

Figure 5.14: PHP image filter for converting image into gray scale

- **Image Histogram**

The standardized image will be fed to the Image histogram phase. At this stage, the system generates the scaled histogram of the input image and stores it in a temporary feature database. We used the histogram technique to address the problem of image segmentation of the ROIs (region of interests). This feature distinguishes our system from other systems.

In the Image processing stage, a histogram is considered a statistical feature, that explains the intensity distribution in an image (Gonzalez & Woods, 1992). The major feature of the histogram is that it can be rapidly saved, controlled, resized, and rotated.

The histogram in a retrieval system needs the following components to function: adequate colour spaces like L*a*b*, L*u*v* or HSV (hue, saturation, value); a similarity metric such as Euclidean Distance (L2) or Matusita distance; and an Intersection method for histograms (Gonzalez & Woods, 2002).

A histogram is produced by dividing a space of colour into numerous bins and by tracking the volume of pixels of the picture that belongs to each bin. To manage an image retrieval system satisfactorily, the various areas that the colour space is separated into is large, therefore, the colours indicated by neighboring areas have relatively small distinctions (Konstantinidis et al., 2005).

The histogram includes a number of levels of pixels in an image that are converted into a fixed number of bins to show the pixels and the intensity value. Each pixel is assigned to a special histogram bin based on the pixel's colour. As mentioned above, the gray scale shown as a distribution of 256 bins. The histogram is one of the important techniques used in content-based image retrieval (CBIR) as it deals with colour or hue correlations (Liu & Yang, 2013).

The ImageMagick tool is applied to generate a histogram in size of (256*200) pixels. Image Magick is a software tool to generate, edit and compose the images in a variety of formats such as GIF, EXR, DPX, PNG, JPEG and TIFF. The functionality of ImageMagick is generally used from the command line or it can use the features from the programs written in any popular language. It can be chosen from different interfaces such as G2F in Ada, MagickCore in C, MagickWand in C, Magick++ in C++, JMagick in Java, MagickNet, in .NET and IMagick in PHP. ImageMagick is used to change or create images dynamically and automatically with a language interface.

ImageMagik is an image-to-image converter. This tool converts the image in a special format to any other image format. It is designed for batch image processing. It includes a library of algorithms for image processing, which are accessible with a special command line. Figure 5.15 shows a sample of a generated histogram from a hand X-ray image. Gray scale images have 256 different intensities, so the generated histograms display 256 distributed pixels between those gray scale values, graphically. When converting a gray scale image to a binary image by thresholding, the histogram determines the value of the threshold to use. The histogram can be bi-model when the image is suitable for thresholding.

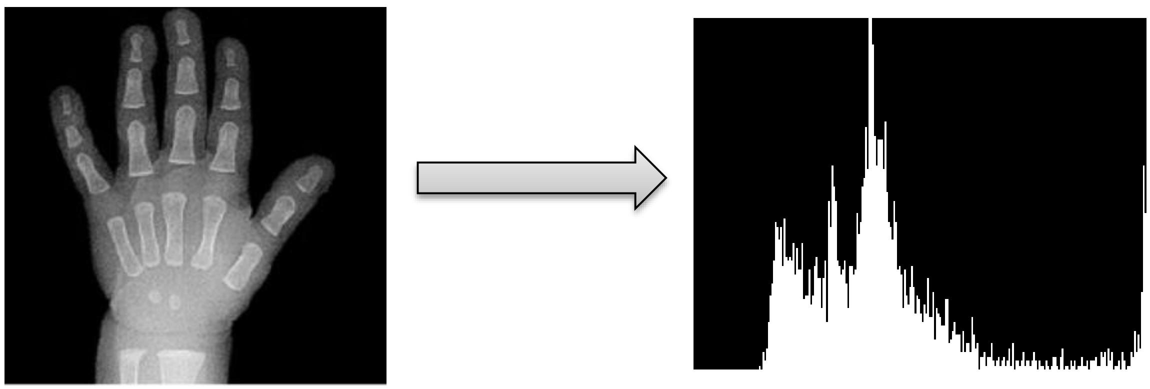

Figure 5.15: A sample of generated Histogram from an X-ray image

The main advantage of the proposed method based on the histogram is the accuracy of retrieval. Search engines retrieve images by comparing the user queries with the shape tags of common features using CBIR method to retrieve the relevant images. A general CBIR system does not cover or is responsible for the resolution, size, and special colour or hue distribution of the images (Arjunan & Kumar, 2009). This limitation would affect our system, especially, the hue distribution of the image, since the ROIs that need to be isolated, have limited accuracy if the hues in the images are not accounted for. The potential for false positives within the standard CBIR systems is due to the use of either the content alone or relying entirely on the metadata of the images. Therefore, in the proposed system, we used a hybrid metadata content approach that relies on histograms for our CBIR. The use of histograms allows the system to account for the colour space, specifically, red, green, and blue (RGB). Since we are dealing with gray scale images it is not of great benefit, but, most importantly, the histogram approach is responsible for variations in the hue, saturation, and value (HSV) space. The total number of bins within the histogram is directly proportional to the discrimination power of the system. Hence, the computational cost of using this approach is justified by the potential for increased accuracy of BAA (Mansourvar et al., 2012).

Therefore, in our proposed system, we generate the histogram instead of extracting the ROIs in the preprocessing stage. This unique feature makes it a new method for bone age assessment. The most important advantage of the histogram technique is the low image preprocessing loading for the system. This leads to an increase in the speed of the bone age estimation process. Our system does not go through the image segmentation process in the image processing stage, unlike other current automated BAA systems.

5.2.3.3 Image processing

The image processing stage is the critical stage for the assessment of bone age. Various techniques are applied in processing the image in order to obtain more accurate estimation of bone age.

The methodology used in our system for image processing is the content-based image retrieval (CBIR) technique. The CBIR technique has become very popular in recent years in medical imaging, and in crime prevention.

The CBIR system was developed to solve the problems encountered with text-based image retrieval in the 1990s. One of the well-known CBIR systems was introduced by IBM in 1995, and it was able to retrieve images based on colour layout and textures occurrence.

In the CBIR system, image retrieval is performed by using extracted features from the visual contents, automatically. The CBIR approach is based on the query by image, and the system measures the similarity among the queries, and then the specific image feature would be retrieved (Gudivada & Raghavan, 1995). The advantage of the CBIR system is accurate features retrieval like shape, colour, region and texture, of the relevant images from the large image database.

- **Image Features**

The primary process in the CBIR system is the construction of a suitable index to the knowledge base. The construction of a CBIR index starts with the extraction of a fitting visual feature from the available images. The visual feature is the basis of the CBIR technique. Different systems have been developed and designed for extracting various types of visual features in the images. Typically, a CBIR system tries to find the best visual features to show different types of images for productive retrieval.

Our proposed system used the histogram for the individual query to the database. In the preprocessing stage, after uploading an image (X-ray radiograph of the hand or clavicle), the histogram of the image as its feature is built and stored in the temporary feature database.

In an image query its histogram is generated, and the search is based on similarity, and the retrieval results are ranked according to a similarity index. Figure 5.16 shows the workflow of the CBIR approach used in our system.

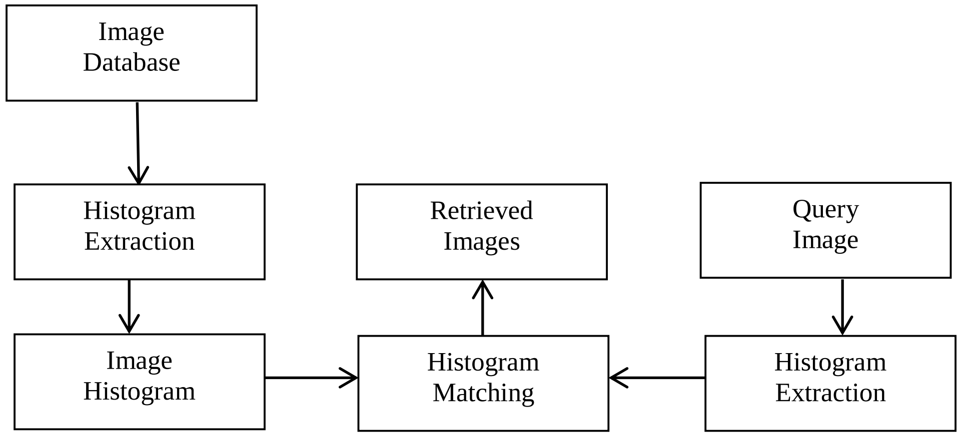

Figure 5.16: CBIR method in BAASHC

- **Content-based image retrieval (CBIR) Histogram**

The histograms explain the proportion of each pixel of colour in the image based on a computationally efficient method. Ballard presented the histogram technique in CBIR system for the first time in 1991 (Lei et al., 1999). The histogram is generated by quantisizing the image into distinct levels and considering the number of repetition each distinct pixel that happens in the images. Therefore, in the retrieval step, the histogram of an image query is compared with the other histograms obtained from all the images in the knowledgebase.

The image processing methods used in the current automated systems, reviewed in Chapter 2, use segmentation techniques for ROIs to find the specific bone edges in the hand images. These methods increase the traffic load in image processing. In addition, the accuracy from the legal aspect, must be considered because of the limitations in the segmentation techniques.

This is the reason why a number of algorithms based on the hand-wrist bones, mentioned in the literature, face the problem of segmentation of special regions in the X-ray image. In addition, and the lack of sufficient image processing techniques leads to low accuracy in the assessment of bone age (Tristan & Arribas, 2008).

The histogram is used throughout the development of our system. This innovative approach is a big improvement on the methods used for estimation of bone age, without the need for image segmentation. In the image processing stage, the system evaluates the X-ray image equally as one complex image.

The image processing functions in our system are divided to four stages:

- Finding similarity;
- Ranking;
- Compression;
- Retrieve images.

The proposed system evaluates the radiograph based on the closest similarity to the retrieved samples. It means that the result is derived from the closest similarity to the earlier samples. This similarity matching is achieved by using a content- based image retrieval (CBIR) system and the bone age is effected visually with what the system computes as the best correspondences to the in the database.

The histogram of an image query is generated and then the search starts using similarity matching, and the output is ranked based on the similarity index.

- **Image comparison using a CBIR engine**

For each ranked image, a unique query is applied. Each query is submitted to the CBIR engine, which will compare the submitted histogram with all histograms in the feature database. Technically, the same label histograms are compared, for example, if the input case is a hand of an Asian female, the system will only retrieve the histogram in the Asian female category of the knowledge base. The different features of the images such as race and sex for hand cases, and left or right position for clavicle images, serve as the standard features for image comparison.

When similar histograms are selected, ranked and submitted to the CBIR engine for comparison, it indicates that the best image has been retrieved for estimation of bone age. The class ImageCompare.php is used for image comparison. Figure 5.17 shows some section of this class for image comparison:

```
$rgb = imagecolorat($im, $width, $height);
$r1 = ($rgb >> 16) & 0xFF; // Hexa value for RED Color
$g1 = ($rgb >> 8) & 0xFF; // Hexa Value for Green Color
$b1 = $rgb & 0xFF; // Hexa Value of Blue Coloe
$rgb = imagecolorat($im2, $width, $height);
$r2 = ($rgb >> 16) & 0xFF;
$g2 = ($rgb >> 8) & 0xFF;
$b2 = $rgb & 0xFF;
 if (!($r1>=$r2 && $r1<=$r2))
$OutOfSpec++;
 if (!($g1>=$g2 && $g1<=$g2))
$OutOfSpec++;
 if (!($b1>=$b2 && $b1<=$b2))
$OutOfSpec++;
 $TotalPixelsWithColors = (imagesx($im)*imagesy($im))*3;
 $Result['PixelsByColors'] = $TotalPixelsWithColors;
$Result['PixelsOutOfSpec'] = $OutOfSpec;
 if ($OutOfSpec!=0 && $TotalPixelsWithColors!=0)
{
$PercentOut = ($OutOfSpec/$TotalPixelsWithColors)*100;
$Result['PercentDifference']=$PercentOut;
$Result['PercentSimilar']=100.0-$PercentOut;
}else{
        $Result['PercentDifference']=0.0;
        $Result['PercentSimilar']=100.0;
        } return $Result;
```

Comparison in RGB Space

Figure 5.17: Part of class ImageCompare.php

Image retrieval using content and metadata produces more accurate result than image retrieval using shape, colour or texture. Most image retrieval systems work with the usual features, but there are false positives in searching similar images. Hence, our system provides a new approach in image retrieval for bone age assessment by using content and metadata together with the histogram (Mansourvar et al., 2012).

Each pixel in the image is defined by three parts in a specific colour space: red, green, and blue in RGB space. A histogram, as a collection of pixels for each quantisized bin, is determined for each part. Obviously, the more bins a colour histogram includes, the more the discrimination power. Hence, a histogram with a large number of bins not only improves the computational cost, but also helps to create effective indexes in the image database.

5.2.3.4 Database

A database model is the template for databases that defines the logical structure of the databases in the system and also explains the manner in which data could be stored, organized, and manipulated. The relational database model is used in this system.

The relational model for database management defines the logical structure of a database. In the relational model, a database is based on a collection of data items ordered by a set of formally-described tables. This model was first proposed by Codd (1970). Data can be accessed or reassembled in many different ways without having to reorganize the database tables in the relational database. The tables are a collection of records and each record in a table contains the same fields. The main features of this model are that it is simple, it has all the properties and capabilities required to process data, and storage efficiency (Meijer & Bierman, 2011). The aim of the relational model is to provide a declarative model for specifying data and queries. Users state what information the database contains and what information they want from it, directly.

In the relational model, all data are stored in relations or tables. The database in our system consists of five main tables: - the first table contains the X-ray images of hand-wrist bone; the second table contains the X-ray images of the clavicle bone; the third table stores the data for related reports; and the remaining two tables used to store the feature images. Figure 5.18 shows the entity relationship diagram (ERD) for this database.

Hand-wrist Table

No.	Column	Type
1	Img_id	Int
2	Age_years	Double
3	Gender	Varchar
4	Ethnic	Varchar

Report Table

No.	Column	Type
1	Img_id	Int
2	Fname	Text
3	Lname	Text
4	Gender	Varchar
5	Ethnic	Varchar
6	Age_years	Double
7	Direct	Varchar
8	Reporttyape	Varchar

Clavicle Table

No.	Column	Type
1	Img_id	Int
2	Age_years	Double
3	Direct	Varchar

Hand-wrist Feature Table

No.	Column	Type
1	Img_id	Int
2	Age_years	Double
3	Gender	Varchar
4	Ethnic	Varchar

Clavicle Feature Table

No.	Column	Type
1	Img_id	Int
2	Age_years	Double
3	Direct	Varchar

Figure 5.18: Entity Relationship Diagram (ERD) of Database

- **Hand-wrist table**

Based on the findings from the questionnaire survey, discussed in Chapter 4, estimation of bone age is affected by gender and ethnicity of the patients. It is, therefore, not surprising that 52.8% of respondents said that race of patients affects the diagnosis of bone age and 88.9% of respondents stated that gender can affect the assessment of skeletal age.

Hence, our hand-wrist dataset is categorized by gender and ethnic origin. The table for hand images contains of 1100 X-ray images from a collection provided by the Medical Image Research Center - IRMA Centre - (Miguel et al., 2003). The IRMA Centre is a cooperative research centre in the Department of Medical Informatics, Division of Medical Image Processing and Computer Science at the Aachen University of Technology (RWTH Aachen).

The data is divided into 551 images of male and 549 images of females hand-wrist. From the review of the literature it is clear that an updated dataset is crucial for developing an automated system for bone age assessment to obtain more accurate and more reliable results (Gertych et al., 2001).

Altogether, the hand-wrist dataset has eight classes:

- Asian-Female (ASF);
- Asian Male (ASM);
- African-American Female (AAF) ;
- African-American Male (AAM);
- Caucasian Female (CAF);
- Caucasian Male (CAM);
- Hispanic Female (HIF); and

- Hispanic Male (HIM).

The data for each class includes 18 age groups, from 1 to 18. Table 5.2 shows the information of the first dataset.

Table 5.2: The detail information of hand images

Ethnicity	Female	Male
Asian	136	137
African-American	139	140
Caucasian	138	136
Hispanic	136	138
Total	549	551

- **Clavicle table**

The second table in our database is a collection of clavicle images. These images were collected from the Picture Archiving and Communication System (PACS) of University of Malaya Medical Centre (UMMC). PACS is network software in UMMC that saves all the medical images for the referees or patients together with their personal information such as name, sex, and age. The PACS system was implemented in UMMC three years ago.

Data was collected over two days in UMMC in March 2013. The second table includes 399 X-ray images of the clavicle. The data is divided into 215 images of the left clavicle, and 184 images of the right clavicle. The data for each category includes various age groups from 2 years to 70 years. As mentioned previously the PACS system was set up in UMMC in 2010, therefore there is no organized information for our dataset like the first dataset.

- **Feature table**

The feature table is the space for storing the histograms in the system. There are two groups of feature data in BAASHC:

- Feature data of hand images; and
- Feature data of clavicle images.

The feature data of hand images can be divided into four groups. Each group includes the histogram of one race, and this is further divided to two sections - male and female.

The feature data of clavicle images is divided into two groups - right clavicle images and left clavicle images.

- **Report table**

The report table stores the data to generate the reports based on the requirements of the users. Section 5.2.4.3 will present more information about the reports facilities in the BAASHC.

5.2.4 Implementation phase

The implementation phase involves more processes besides the materials developed. This phase involves the continuous modification of the program to ensure system efficiency to produce positive results. This phase includes evaluation of the design phase.

5.2.4.1 Age estimation

The main step in implementation a computerized system for BAA is the process of estimating the bone age using an automated technique based on the hand images or clavicle images. Bone age in our system is assessed by comparing the image with images in the repository, which that are sample cases from people of various age and from both genders and of different races. This process is similar to other BAA systems but with the difference that our proposed system, unlike the other BAA systems, uses histograms as the feature in image processing.

Rather than merely extracting the image features for comparison, our proposed system converts the image into a histogram for comparison with the standard sample histograms in the database, and all histograms with potentially high similarity will be retrieved and stored in a temporary feature database. The temporary database is necessary for ranking the retrieved images. The tagged age values of the retrieved image are used as part of the BAA process and the final estimated bone age is obtained as the mean of the retrieved values:

$$\text{Estimated Bone Age} = \frac{\sum_{i=1}^{n} x}{n}$$

Where $x = Age\ of\ highest\ ranked\ retrieved\ images$,
$n = Total\ number\ of\ highest\ ranked\ retrieved\ images$

Therefore, the age estimation process is arranged in three main levels:

1. The histogram is extracted and stored in a temporary directory;
2. Each histogram is used as an individual query to the search engine; and
3. For each query, the best matching case is retrieved from the feature database, based on the similarities score.

Figure 5.19 illustrates the workflow of the BAA processes in the proposed system:

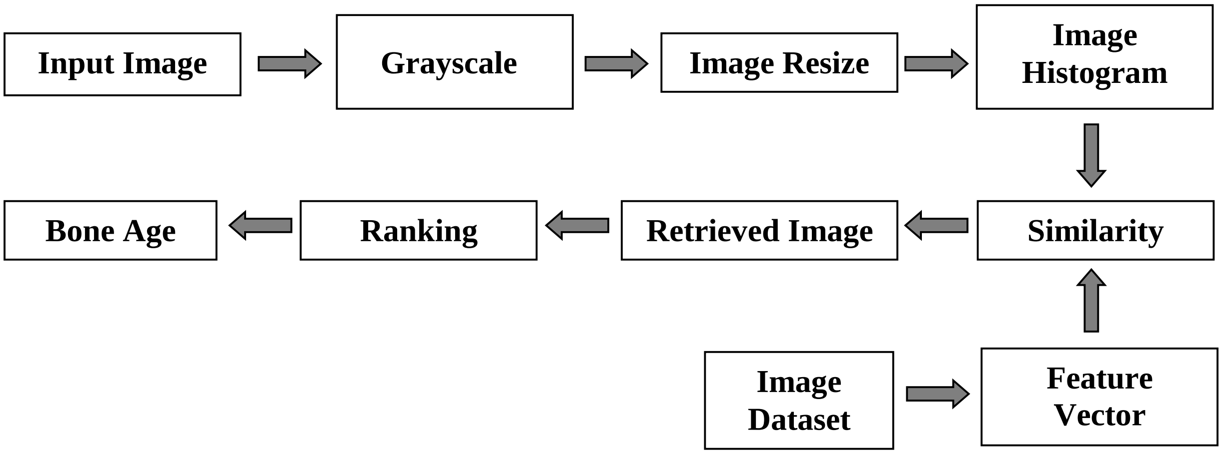

Figure 5.19: System processes for bone age assessment

Figures 5.20-5.21 show the screenshots of the pages when a user is uploading a new case of estimation of bone age. If the new case is a hand-wrist image as shown in Figure 5.19 the user should provide the name, last name, gender, and ethnicity of the patient. If the new case is a clavicle image, the user should provide the name, last name, and the direction of the image.

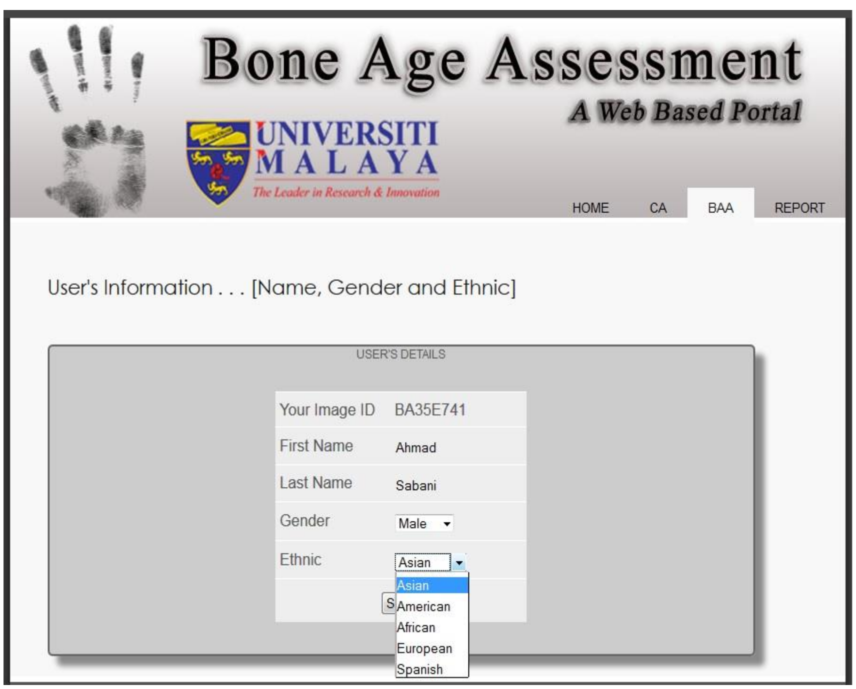

Figure 5.20: The page of inserting user information for hand images

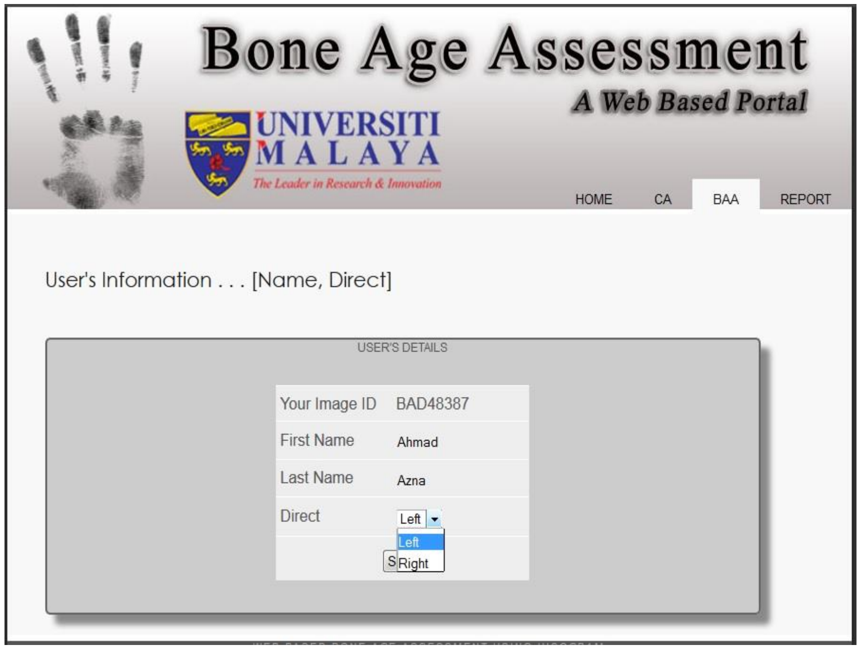

Figure 5.21: The page of inserting user information for clavicle images

After uploading the image, and inserting the patient's information and saving the case, the system starts to process the image, as discussed in Section 5.2.3.3. The result - the estimated bone age - is displayed after a while about 1 minute. Figures 5.22-5.23 show the result pages for the cases.

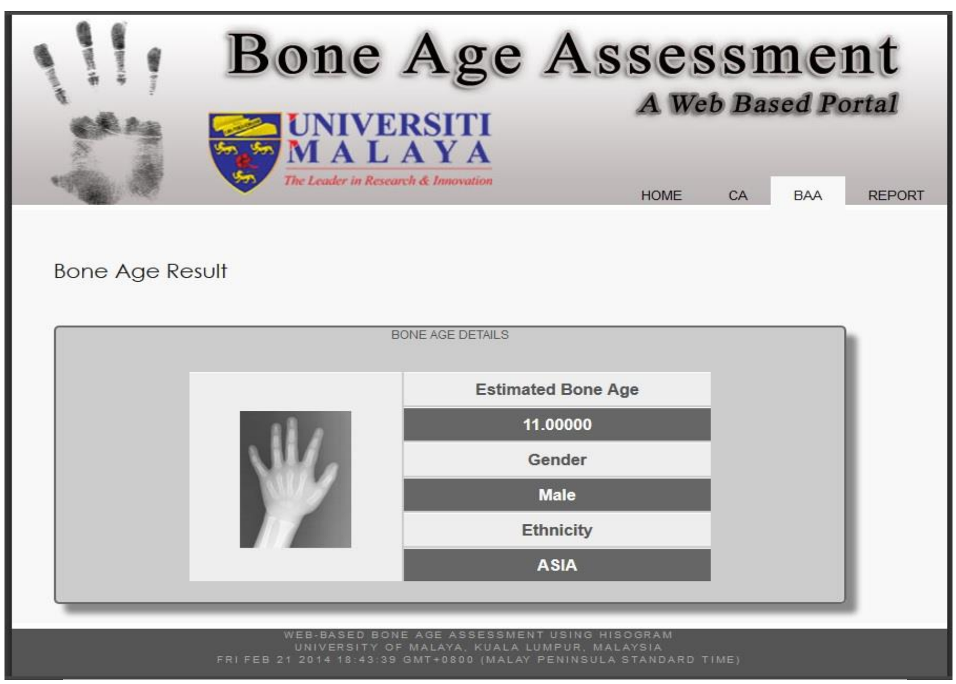

Figure 5.22: Result page for bone age assessment for hand

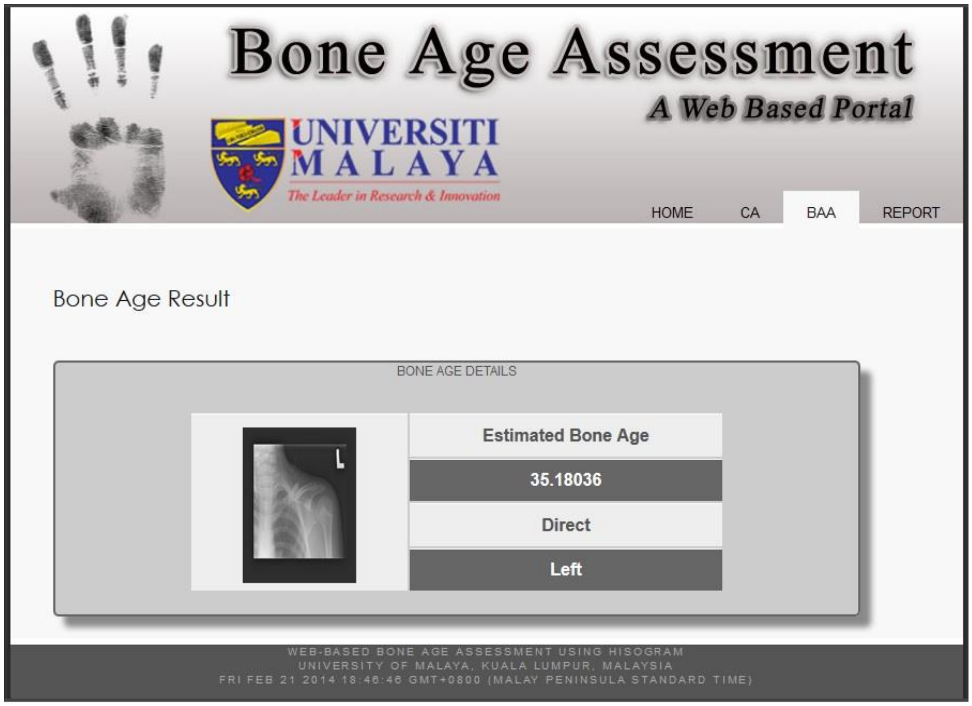

Figure 5.23: Result page for bone age assessment for clavicle case

5.2.4.2 Bone age assessment system using the hand and clavicle bones (BAASHC)

One of the main contributions of our system is the use of images of the hand-wrist bone together with the clavicle bone to provide more accurate estimation of bone age. The workflow of the proposed system is shown in Figure 5.24.

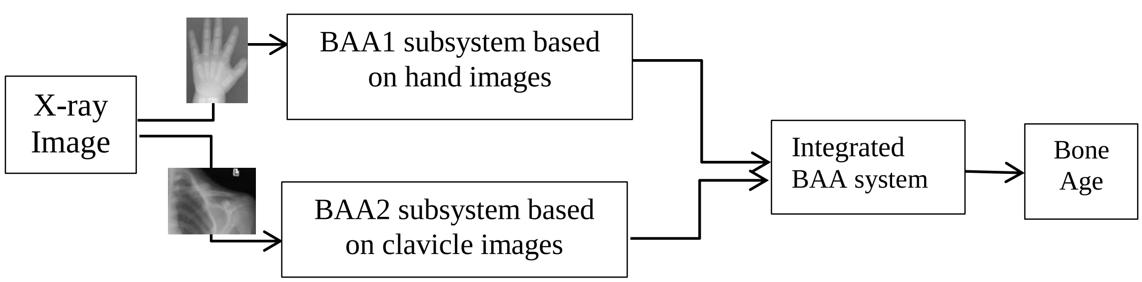

Figure 5.24: Workflow for BAASHC

Subsystem BAA1 was designed to process hand images and subsystem BAA2 was designed to process clavicle images. BAA1 and BAA2 subsystems are merged into the final BAA system, BAASHC.

In normal cases, the use of hand images produces accurate age estimation of patients, age estimation of both girls and boys of up to 18 years of age and with normal skeletal growth. If hand images of unknown cases cannot be detected. Then this is caused by very noisy images, abnormalities in skeletal development, injury to the hands, hence the BAA2 subsystem can be used. The BAA2 subsystem is presently at the preliminary stage of development. This subsystem is designed using a limited number of clavicle images from the University of Malaya Medical Centre (UMMC) of the local samples.

5.2.4.3 Structure of BAASHC report

The system was designed to facilitate the work of radiologists or doctors conducting BAA at UMMC, and meet all the requirements in an automated BAA system based on their feedback to the questionnaire survey and interviews.

The results of the questionnaire survey indicate that the better management of patients' information to achieve efficiency and effectiveness is one of the requirements for BAA system - it achieves score of 4. This means that the proposed automated system should save the patient's information pertaining to their bone age estimation, so that it can be used as reference for other BAA cases.

In order to incorporate this feature into the system, a structure of the BAASHC report is provided. The BAASHC is a standalone system for bone age assessment and it accepts the X-ray images of the hand or clavicle and processes the images to output the estimated bone age.

This automated system eliminates the need to make visual observation and it assists the radiologists to obtain more accurate estimation of bone age, and brings manages BAA information of patients more efficiently and effectively in the clinical environment.

The structure of the BAASHC report is used to store and display the following types of information of the patient:

- Bone Age Assessment based on image of the hand;
- Bone Age Assessment based on image of the clavicle; and
- Bone Age Assessment by the radiologist.

For a given X-ray image of the hand and the clavicle together with the patient information, the BAASHC system generates a BAA report that includes three classes, as shown in Figure 5.25.

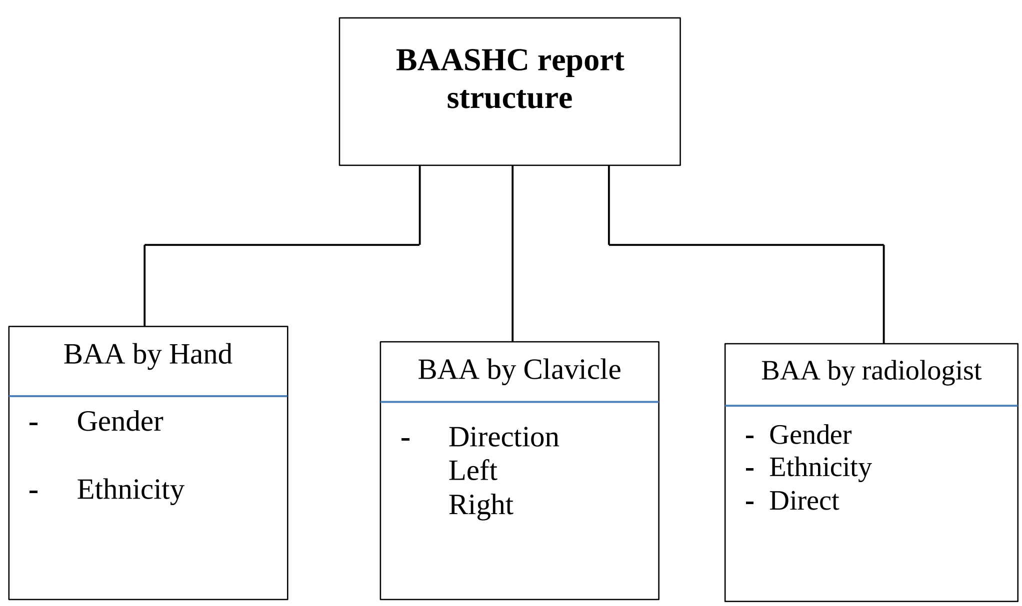

Figure 5.25: Structure of BAASHC report.

The first type of report is bone age assessment based on the hand image, and includes the patient's race, and gender. The BAASHC system assesses bone age automatically, and saves the result for further reference. The second type of report is bone age assessment based on the clavicle image, and it displays the position of the clavicle bone – right clavicle or left clavicle. Bone age estimation based on the clavicle image is also done automatically. The third type of system report is bone age assessment by the radiologist who is involved in assessing the patient's hand image and also the clavicle image. The radiologist or the expert who works with the system is able to save his/her estimation of bone age in the system. By using this feature, the specialist in BAA can compare his/her estimation of bone age with the estimation of bone age generated by the system.

Figure 5.26 shows the pages when the user selects bone age assessment by the radiologist in boneage.php.

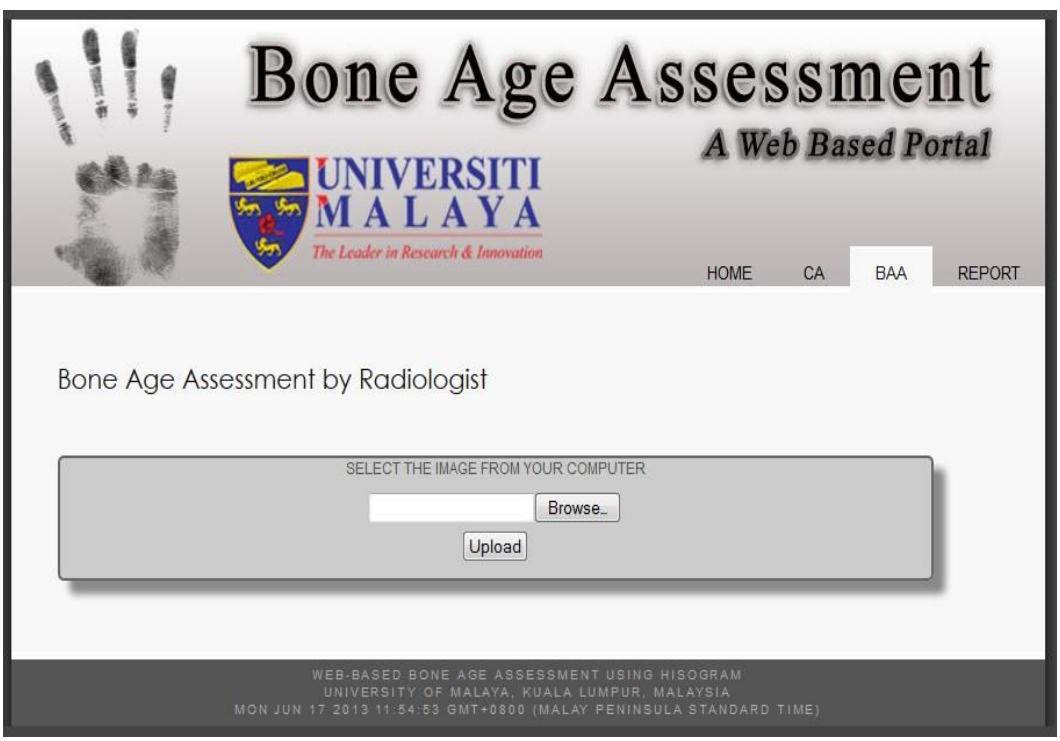

Figure 5.26: The page of BAA by radiologist

In this page (Figure 5.27) the radiologist can upload the hand-wrist image or the clavicle image for estimation of bone age. The image cropping page will then be loaded. By clicking on the next button, the page for inserting the user's information is displayed, as shown in Figure 5.28. The radiologist inserts the patients' data that is linked to the uploaded image. For example, if the uploaded image is the hand image the radiologist inserts the patient's first name, last name, races and gender. If the uploaded image, is clavicle image information about the direction of the clavicle bone should be filled. The last field is for the estimated age, based on the assessment and experience of the radiologist. After saving the data, the radiologist will receive the message from the system that the information is saved successfully, as shown in Figure 5.29.

Figure 5.27: The page for uploading image by radiologist

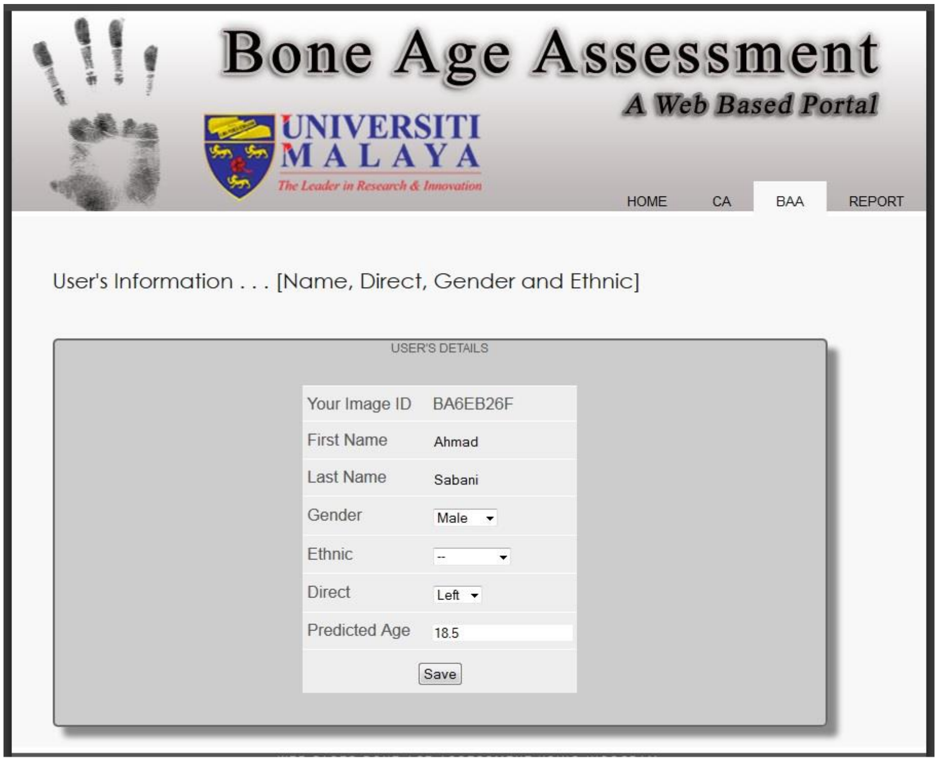

Figure 5.28: The page for inserting the user's information

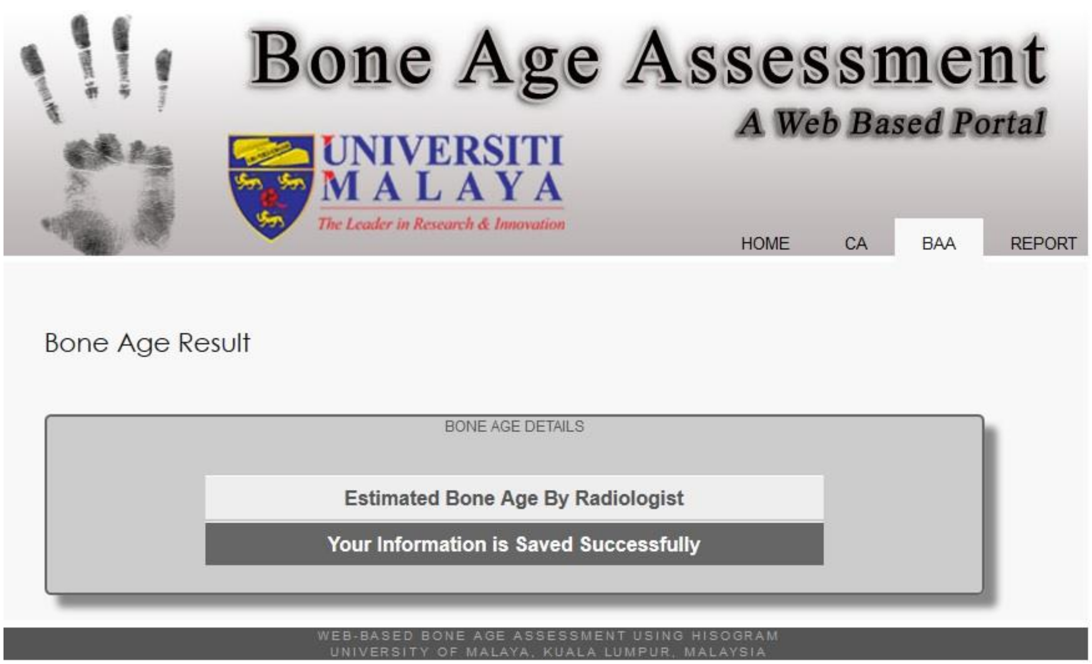

Figure 5.29: The message for saving data successfully

The proposed system has a user-friendly report system. The reporting facility allows the saved information to be accessed or to be compared with the estimated bone age output by the system with the estimated bone age by a radiologist. In the report page, the user inputs the patient's information including the first name, and the last name as shown in Figure 5.30. Figure 5.31 shows the results of a bone age assessment case done previously. This shows if a patient's age has been estimated by the system previously, the information and the results have also saved for the next retrieval. The table of the report in the main database consists of a set of records of user' information that is responsible for the report structure in the system.

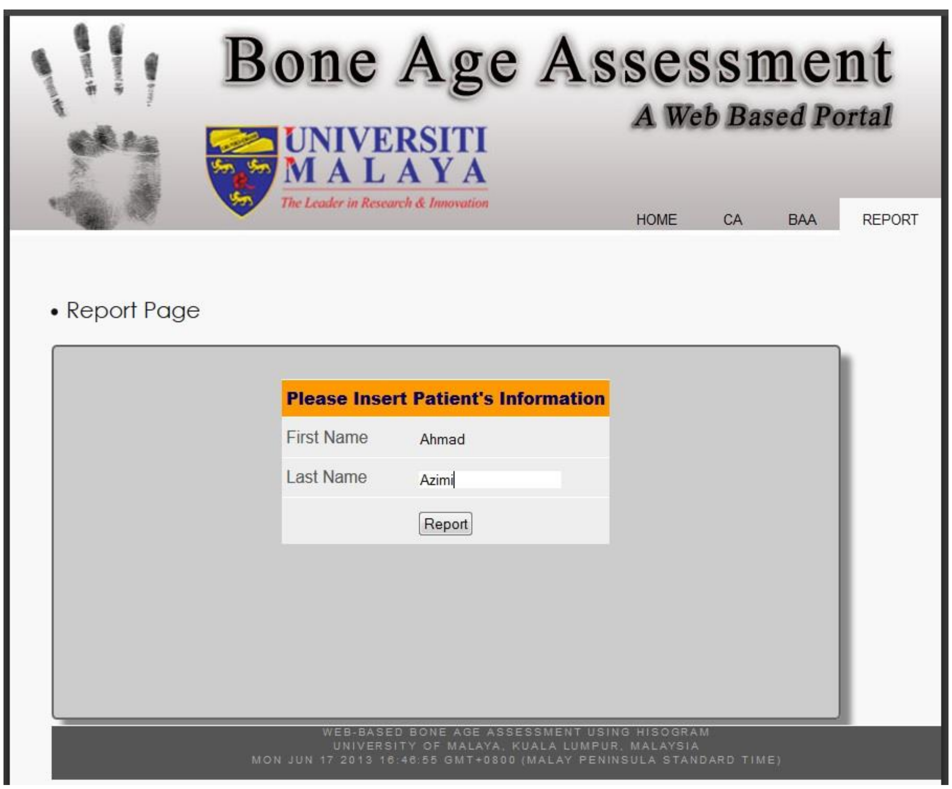

Figure 5.30: The report page

Figure 5.31: The page of report result

5.2.4.4 Chronological age assessment

Another feature which is incorporated into this system is a facility for the assessment of chronological age. As mentioned in the previous chapter, one of the applications of bone age assessment is monitoring growth, and endocrine disorders. It means that any difference between chronological age and bone age could be an indication of abnormality in skeletal development (Giordano et al., 2011).

In this page, radiologist inputs the date of birth of the patient, and the date of testing. The system would then calculate the chronological age in years and months, as shown in Figure 5.32.

A specialist is able to detect whether bone growth has been delayed, by comparing of the chronological age with the estimated bone age by the system.

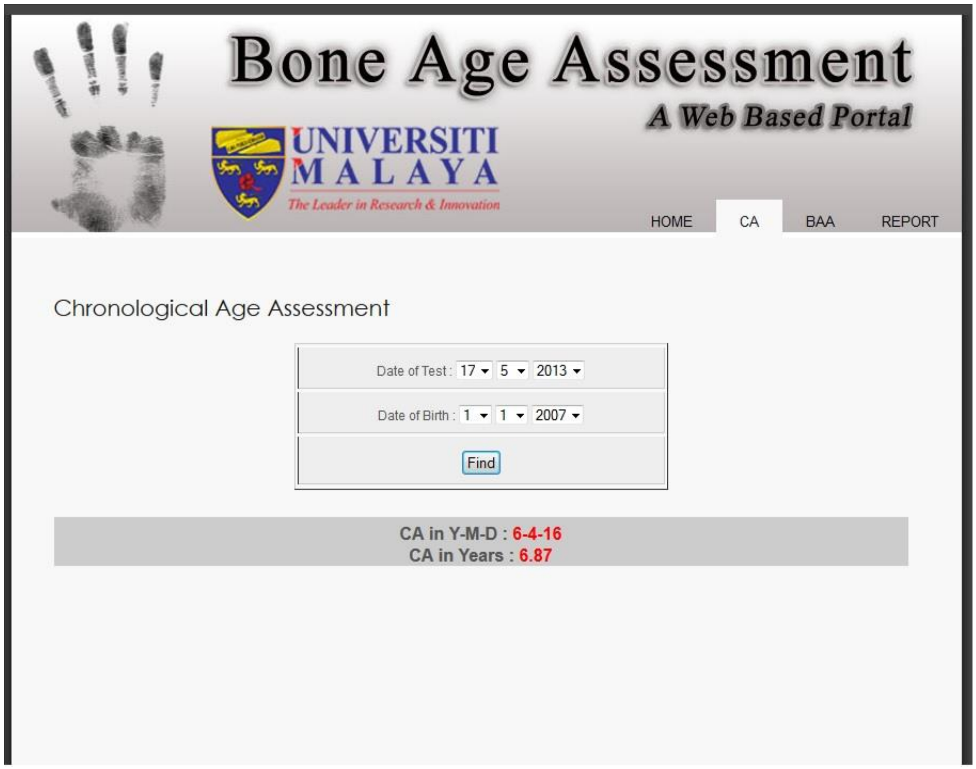

Figure 5.32: The page for assessment of CA

5.2.5 Evaluation phase

In the evaluation phase of the ADDIE the BAASHC system subjected to final testing to determine whether the requirements and overall objectives have been achieved. This stage consists of two parts - formative and summative. Formative evaluation has been carried out at each stage of the ADDIE developmental processes. In formative evaluation the accuracy of system in terms of assessment the age is tested. In summative evaluation the end-users are given the opportunity to provide feedback on whether their requirements have been met. The results of the evaluation phase will be presented in the next chapter.

5.3 Summary

This chapter discusses the development of an automated system to assess bone age based on the hand and clavicle images. The system called, BAASHC was developed based on the ADDIE model and took into consideration all the users' requirements based on the feedback to a questionnaire survey and the interviews.

A computerized system for BAA can assist the radiologists and experts to estimate the bone age faster and more accurately. Furthermore, the system also helps to reduce costs in the clinical environment, saves time and, is easy to use. This system eliminates the variability of human observation which had been the main cause for low accuracy in the estimation of bone age in the manual methods.

In this research, a new method for bone age assessment using the histogram technique was proposed. This method is a new way of processing X-ray images. Existing automated BAA systems such as the system proposed by Spampinato et al (2010), BoneXpert System by Thodberg (2009), the system proposed by Trist and Arribas (2008), system by Liu et al. (2008), Mahmoodi model (2000) Phalanges Length- based System by Pietka, Gertych, and Huange (1990**),** PROI based-system by Pietka et.al. (1991), CASAS system by Tanner and Gibbons(1994), Middle phalanx of the third finger by Niemeijer (1995), …..etc., applied segmentation of regions of interest (ROIs) in their image processing technique. The weaknesses in these systems are the need for segmentation of specific regions in the radiograph, and the lack of suitable image processing techniques. Our system generates histograms for use in assessing the bone age. The histogram of the image is used as an indicator to detect the unknown bone image. The image is tagged with a corresponding profile and stored in a database. To estimate the bone age, a corresponding image histogram of the radiograph is created and compared with the histograms stored in the feature knowledgebase. The age of the bone is estimated based on the closest matching of the image histogram to other bone image histograms. This method overcomes the segmentation problem encountered in other BAA systems.

In addition, our system used both the hand and clavicle images for bone age assessment. This approach overcomes the problem of very noisy hand images that can affect accuracy in the estimation of bone age. This new feature enables the doctors to assess the bone age of people who have growth abnormality of their hand or other hand injuries. Therefore, this system not only useful in the daily clinical practice but is also useful to forensic experts.

The BAASHC is a web-based system and is publicly available, and PHP is used to interface the MYSQL database. Our system uses content-based image retrieval (CBIR) technique in order to compare the images based on the image content and metadata, using the respective histograms of the images to increase sensitivity to primary hues. Content-based image retrieval, also called query by image content, is applied in computer vision to solve the image retrieval problem encountered in a large image database.

The database of our system consists of two main tables: the first table contains 1100 X-ray images of the hand-wrist from a collection provided by the Medical Image Research Centre (IRMA), and the second table contains 399 X-ray images of the clavicle collected by the University of Malaya Medical Centre (UMMC).

Chapter 6 will present the evaluation of BAASHC in terms of the accuracy in assessment of bone age and the usability and performance of the system from the users' perspectives.

Chapter 6: System Evaluation

A program is not considered finished until it has passed its testing (Whittaker, 2000).

6.1 Introduction

System testing is an important process in the development of a system to evaluate the quality and to observe whether the proposed system works as expected in the real environment. The main aim of testing is to evaluate that the system fulfills the specific users' requirements, and overcome the limitations (Beizer, 1984). Therefore, a systematic method of testing is needed to ensure that the system is evaluated fully.

This chapter discusses the comprehensive accuracy evaluation of the BAASHC system. This chapter has two main sections. In the first section, the BAASHC software is statistically analysed and in the second section, it is evaluated by potential users.

Figure 6.1 shows that the evaluation of BAASHC starts from the testing of the two subsystems (BAA1 and BAA2) and followed by overall evaluation of the usability of the whole system.

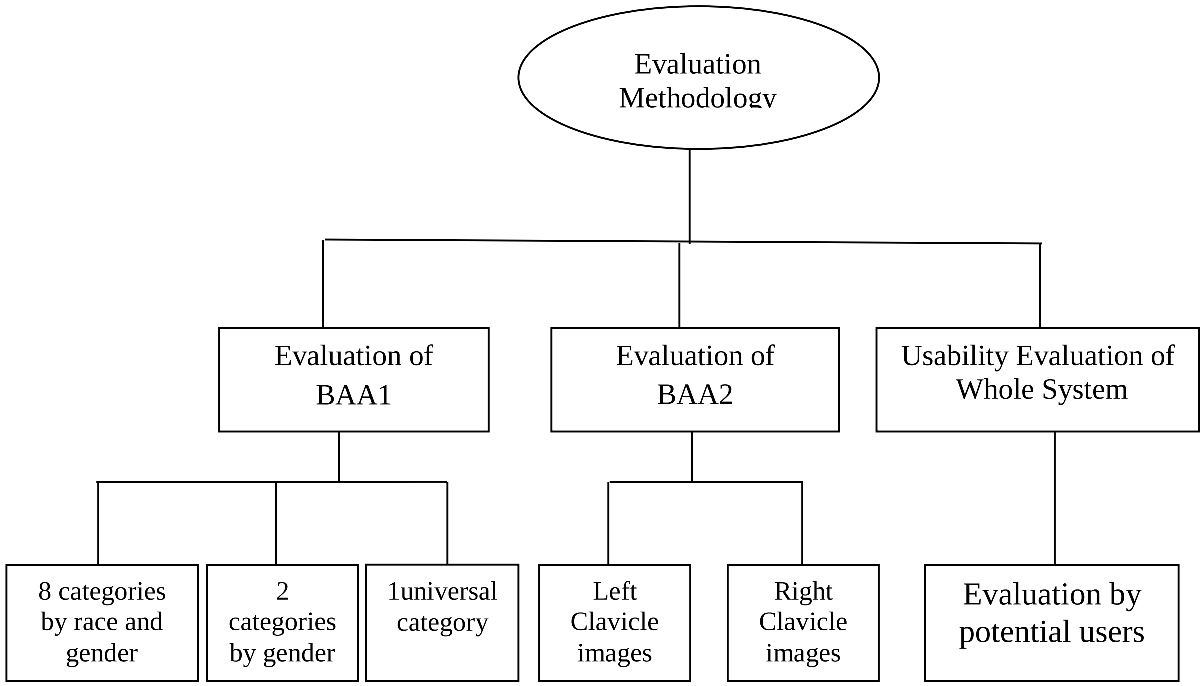

Figure 6.1: Methodology of Evaluation of BAASHC

6.2 Evaluation of BAA1 subsystem

The evaluation of the BAA1 subsystem includes three separate test sections to test the performance of the bone age assessment based on the hand-wrist bones. In Test 1, the sample data is divided into eight categories by gender and by race (Asian Female, Asian Male, African /American Female, African/American Male, Caucasian Female, Caucasian Male, Hispanic Female and Hispanic Male). In Test 2, the sample images are separated into two categories: female and male, and each category include four different races. In Test 3 the sample data are joined into one category.

The bone age results generated by subsystem BAA1 were plotted with the radiologist estimation versus the chronological age of the samples. The mean difference between the radiologist readings and the chronological age (CA) or system estimated bone age versus chronological age is computed by paired t-test as a mean of evaluation.

6.2.1 Plots

The BAA1 subsystem results are compared with the estimated bone age results of a UMMC radiologist who used the GP method. Both results were compared against the chronological age (CA) of the sample data. Figure 6.2 to Figure 6.9 show the results of eight categories from Test 1. The following sections present the details of the statistical analysis.

Figures 6.10-6.11 show the results of two categories of Test 2, and Figure 6.12 shows the result of Test 3 that involves one universal category. All the figures shown is the results of the comparison of age estimation by the radiologist with the chronological age (CA) and also the difference between the generated results by the system with the CA. The following sections present the details of the statistical analysis.

Results from Test 1 with race and gender, separated. In each graph, the solid line represents the system bone age results and the dotted line represents, the chronological age, and dash line the reading of a radiologist.

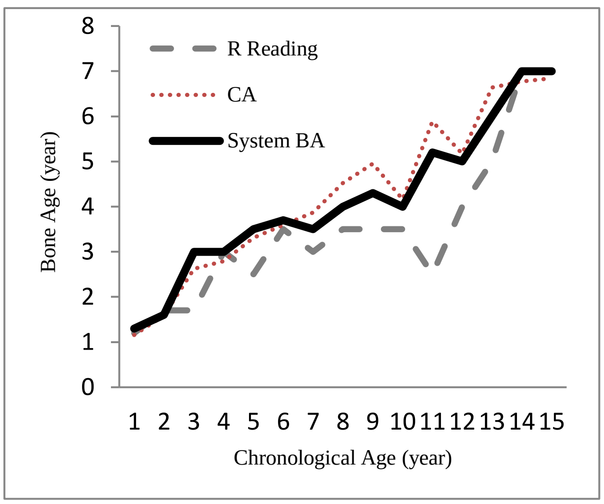

Figure 6.2: Comparison between CA and System estimated BA of Asian females

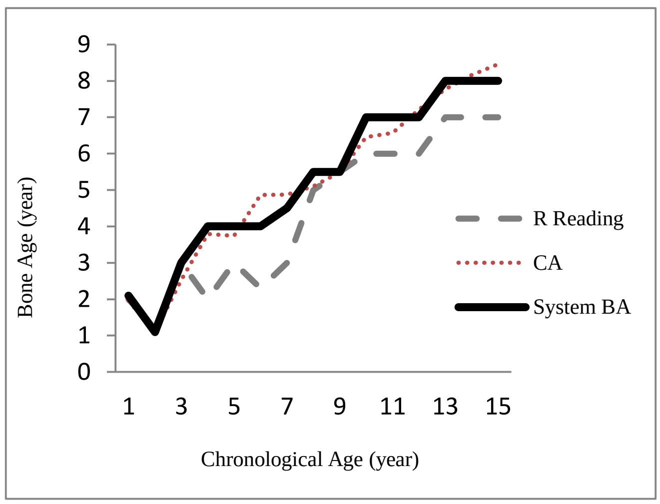

Figure 6.3: Comparison between CA and System estimated BA of Asian males

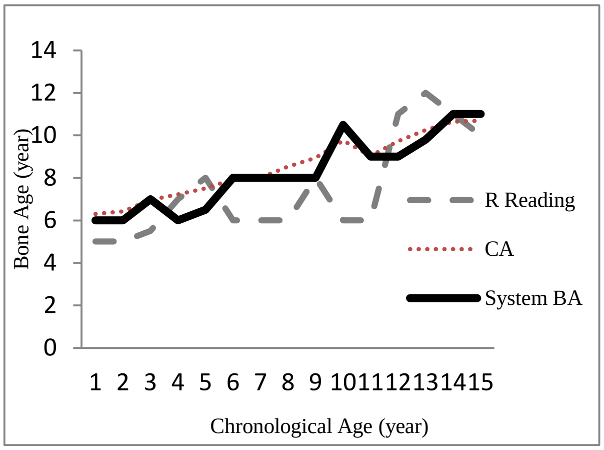

Figure 6.4: Comparison between CA and System BA of African/American female

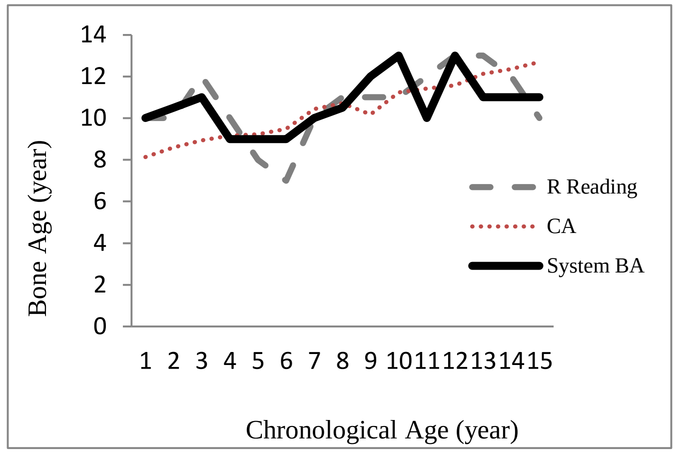

Figure 6.5: Comparison between CA and System BA of African/American male

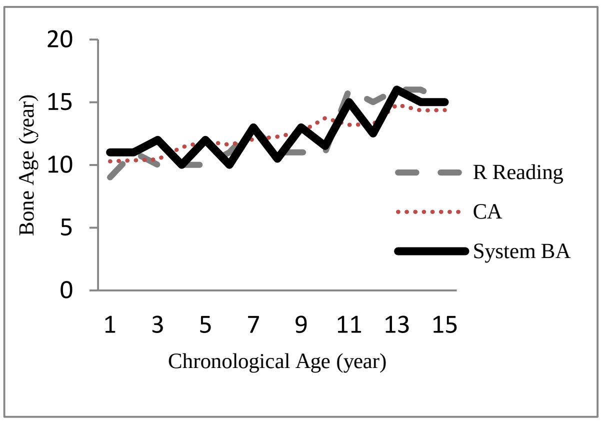

Figure 6.6: Comparison between CA and System BA of Caucasian female

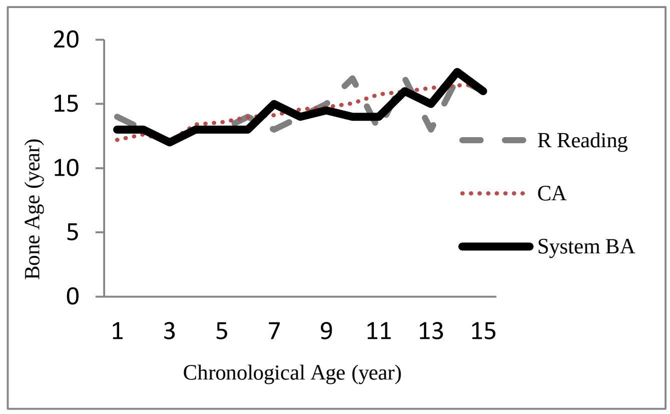

Figure 6.7: Comparison between CA and System BA of Caucasian male

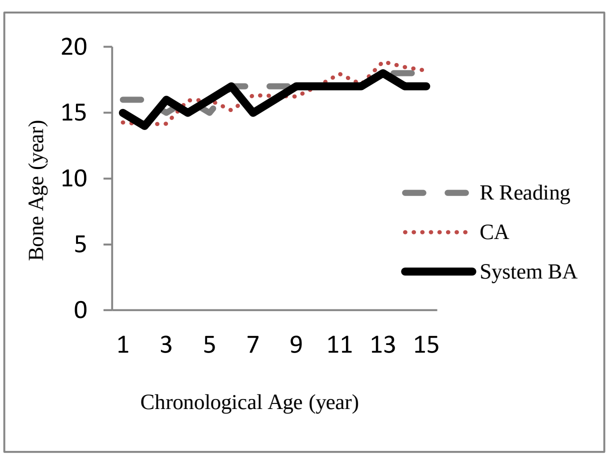

Figure 6.8: Comparison between CA and System BA of Hispanic females

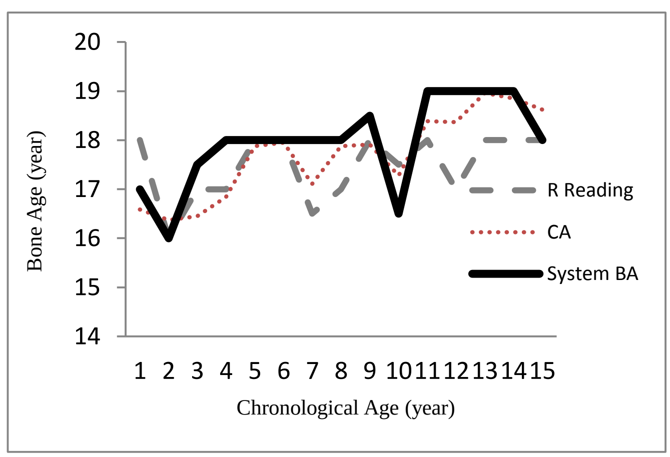

Figure 6.9: Comparison between CA and System BA of Hispanic males

Results from Test 2 for both genders with four races combined: Male and Female. In each graph, the solid line represents the system bone age results and dotted line represents chronological age, and dash line the reading of the radiologist.

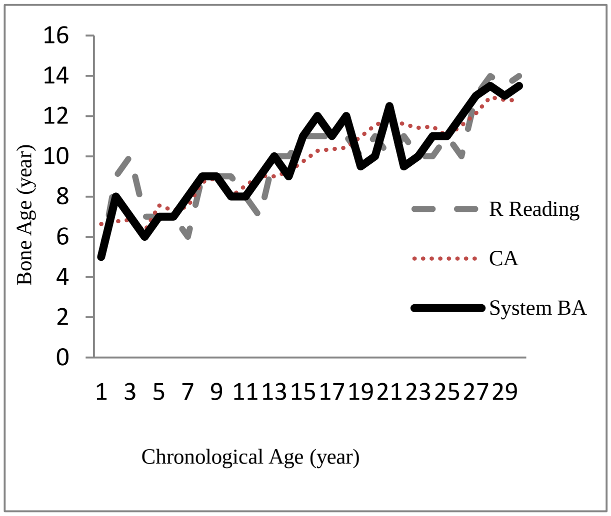

Figure 6.10: Comparison between CA and System BA of females with four ethnics.

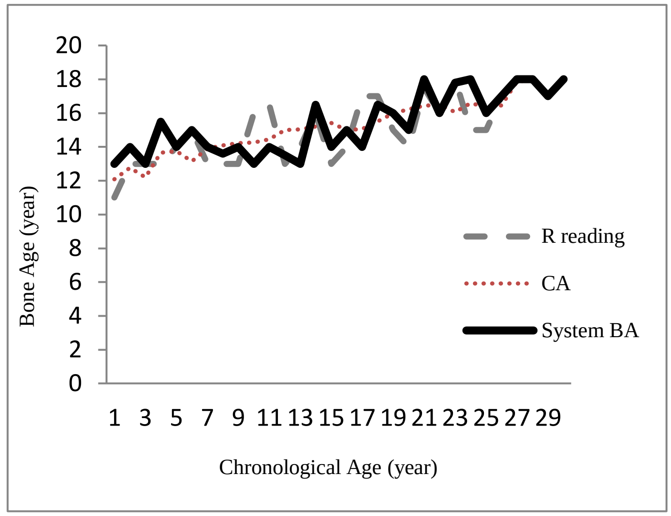

Figure 6.11: Comparison between CA and System BA of males with four ethnics.

Results from Test 3 for one universal category with both genders, and different races. In each graph, the solid line represents the system estimated bone age results, and dotted line represents chronological age, and dash line the reading of a radiologist.

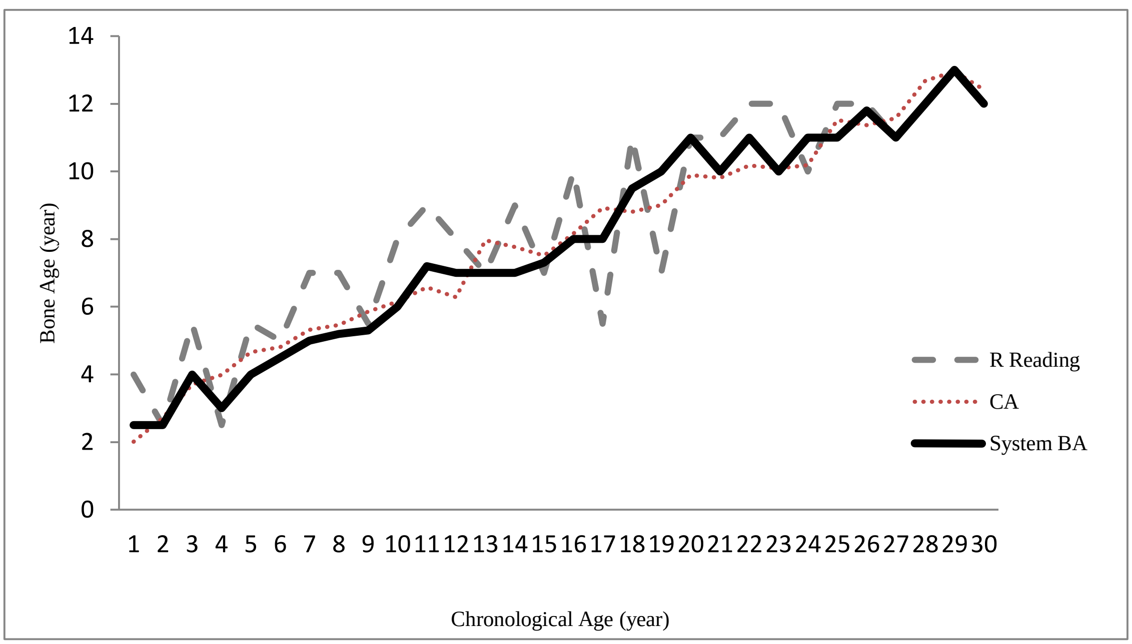

Figure 6.12: Comparison between CA and System BA of universal category

6.2.2 Statistical analysis for Test1

For all three tests, a paired-samples t-test was applied to the chronological age (CA) against the radiologist reading and system estimated bone age (BA). Table 6.1 and Table 6.2 show the mean value and standard deviation (SD) between the radiologist reading and the system estimated bone age (BA) versus the chronological age for Test 1. The p-value was calculated to signify the mean difference of the system estimated bone age and the radiologist reading against the chronological age. The number with asterisk shows that the difference is significant at p-value < .05.

Table 6.1: The difference of mean chronological age and system BA grouped by gender and race for Test 1

Ethnicity	Female					Male				
	Mean (CA)	Mean (BA)	$A_{Difference} = CA_{mean} - BA_{mean}$	Standard Deviation, μ, of $A_{Difference}$	***p*- Value**	Mean (CA)	Mean (BA)	$A_{Difference} = CA_{mean} - BA_{mean}$	Standard Deviation, μ, of $A_{Difference}$	***p*- Value**
Asian	4.2580	4.1400	0.11800	0.36801	**0.235**	5.2040	5.2467	-.04267	.39489	**0.682**
African/ American	4.5000	8.2533	0.75333	1.89128	**0.145**	10.4160	10.6667	.25067	1.39895	**0.499**
Caucasian	12.4353	12.500	.06467	1.28458	**0.848**	14.4853	14.2000	-.28533	.80916	**0.194**
Hispanic	16.4147	16.266	.14800	1.05351	**0.595**	17.6967	18.0000	.30333	.72311	**0.127**

* P-value < .05, significant difference

Table 6.2: The difference of mean chronological age and radiologist reading grouped by gender and race for Test1

Ethnicity	Female					Male				
	Mean (CA)	Mean (RA)	$A_{Difference}$ = $CA_{mean} - RA_{mean}$	Standard Deviation, μ, of $A_{Difference}$	***p*- Value**	Mean (CA)	Mean (RA)	$A_{Difference}$ = $CA_{mean} - RA_{mean}$	Standard Deviation, μ, of $A_{Difference}$	***p*- Value**
Asian	4.2580	3.3867	-.8713	1.06102	**.007***	5.2040	4.4000	-0.80400	0.86231	**0.003***
African/ American	7.5000	8.5273	1.0273	1.55682	**0.023***	10.4160	10.6667	.25067	1.5526	**0.542**
Caucasian	12.4353	12.3333	.1020	1.60487	**0.809**	14.4853	14.2667	.21867	1.4190	**0.560**
Hispanic	16.4147	16.7333	-.3186	.98065	**0.229**	17.6967	17.4667	.23000	.7039	**0.226**

* P-value < .05, significant difference

In Test 1, the Asian samples selected ranges from one year to 6 years for females and from 1 year to 8 years for males. Table 6.1 shows that the system is able to assess the bone age of both genders of the Asian population very accurately.

In one case the chronological age of an Asian female is very close to the system estimated bone age with a mean difference of 0.11800 (Figure 6.2). The graph in Figure 6.3 shows a comparison of the chronological age versus system estimated BA and the radiologist reading. It is evident that the system produces the acceptable result with a low mean error rate of between 0 and 0.8 year and a P-value of 0.682. However, significant difference is observed in the radiologist reading of Asian sample of both genders with P-value of 0.007 for female sample and P-value of 0.003 for males (Table 6.2). These results justifies the subjective decision an age assessment using the GP atlas, as mentioned in Chapter 2 (Roche et al., 1988).

The African/American samples selected consist of those between 6 to 11 years for females and 8 to 12 years for males. Figure 6.4 shows that the system estimated bone age was a little delay, when compared to the CA with the low mean difference of 0.75333 years, except in range from 6 to 10 years.

Table 6.2 shows the significant discrepancies with P-value 0.023 when comparing CA and radiologist reading in the females. Figure 6.5 shows that both system estimated bone age and the radiologist reading produce accurate results for assessment of bone age in African/American males. The results are very similar for system estimated BA and radiologist reading especially in the age range of 8 and 11 years. The mean difference of 0.25067 is similar for system BA and radiologist reading versus CA (Tables 6.1-6.2).

The Caucasian group tested comprised those from 10 to 14 years for females, and from 12 to 16 years for males. In Table 6.1, the system estimated bone age fall within the mean difference of 0.06467 for females, and 0.28533 for males with CA. Results in Table 6.2 also shows that the radiologist reading provides accurate estimation for both males and females. However, the mean difference shows that the system produces more accurate bone age assessment especially in the female group. Hence, any future work on BAA techniques should be aimed at improving the accuracy of assessment for the Caucasian male subset this will be discussed in Chapter 7.

The Hispanic samples chosen include those who age ranges from 14 to 18 years for females and 16 to 18 years, for males. Table 6.1 that the system shows good performance for both genders, with P-value= 0.595 (females) and P-value= 0.226 (males). The system estimated bone age is comparable to the radiologist reading with P-value 0.229 (female), and 0.226 (male) (Table 6.2). However, the mean difference for the male group in the radiologist reading is less than the estimated bone age generated by the system. Furthermore, the system estimated BA and the radiologist reading for females is very similar especially in the age range 17 to 18 years (refer to Figure 6.8). There is difference of about 1.5 years at age 16 years in the system bone age and, about 1 years difference in the radiologist reading (refer to Figure 6.9).

The result of Test 1 shows, however, that the assessment is conducted by an experienced radiologist, but we still observe a significant error in some subsets of the sample, and that the automated system is able to produce more accurate results for various categories. In the next section, the statistical analysis for Test 2 and Test 3 will be discussed.

6.2.3 Statistical analysis for Test 2 and Test 3

In Test 2, the sample data is divided into two groups - female and male. Each category consists of four different races. Test 3 includes 30 sample images with different ranges of age. Table 6.3 to Table 6.4 show the statistical test results for Test 2 and Test 3.

Table 6.3: The difference of mean chronological age versus system BA and radiologist reading grouped by gender in Test 2

Test 2	**CA versus System BA**					**CA versus Radiologist Reading**				
	Mean (CA)	Mean (BA)	$A_{Difference} = CA_{mean} - BA_{mean}$	Standard Deviation, μ, of $A_{Difference}$	***p*-Value**	Mean (CA)	Mean (RA)	$A_{Difference} = CA_{mean} - RA_{mean}$	Standard Deviation, μ, of $A_{Difference}$	***p*-Value**
Female	9.774	9.816	.04233	.96823	**0.812**	9.7743	9.8167	-.04233	1.26118	**0.855**
Male	15.207	15.346	.13900	1.07228	**0.483**	15.2077	15.1000	.10767	1.32130	**0.659**

* P-value < .05, significant difference

Table 6.4: The difference of mean chronological age versus system BA and radiologist reading for 1 universal group in Test 3

Test3	CA versus System BA					CA versus Radiologist Reading				
	Mean (CA)	Mean (BA)	$A_{Difference}$ = CA_{mean} – BA_{mean}	Standard Deviation, μ, of $A_{Difference}$	***p*-Value**	Mean (CA)	Mean (RA)	$A_{Difference}$ = CA_{mean} – RA_{mean}	Standard Deviation, μ, of $A_{Difference}$	***p*-Value**
universal category	7.94 57	7.8933	-.05233	.62023	**0.647**	7.9457	8.4667	-.52100	1.40816	**.052**

* P-value < .05, significant difference

In Test 2, the female sample comprised those from age 6 to 12 years and mixed with four races and for male selected from age 12 to 18 years with mix of four races.

Table 6.3 shows that the estimated bone age by the system fall within the mean difference of 0.04233 years for females, and, 0.13900 year for males, compared with the chronological age. Table 6.3 indicates that radiologist who uses the GP atlas is able to make accurate age estimation, which is comparable to the average estimated age from our system (refer to Figures 6-10 for females, and Figure 6.11 for males).

Finally, the samples for Test 3 are selected in one universal category comprising both genders of four different races. The samples are aged from 2 years to 12 years.

Table 6.4 shows that, that the system produces very accurate estimation of bone age t for one universal category, with a P-value of 0.647. However, the P-value for bone age estimation by the radiologist is bigger than .05, but there is significant difference in the age range of 3 years, 7 years and 10 years (refer to Figure 6.12). These results clearly show the advantage of an automated system over the manual approach, for bone age assessment.

6.2.4 Summary of BAA1 evaluation

The BAA1 subsystem is aimed at assessing bone age by using images of the hand-wrist bones. The BAA1 subsystem was evaluated with three cycles of data. Three different statistical analyses were conducted on the BAA1 results as well as the results of the radiologist reading outcome based on race and gender with the chronological age as the standard. In Test 1, the samples were grouped into eight categories based on female and male, and from four races (Asian, African/ American, Caucasian, and Hispanic). In Test 2 the sample data were grouped in 2 sections according to female and male. Each group contains samples of four races. Test 3 includes one universal group that includes both female and male from four races. In all the tests, the bone age estimate by the system and the age estimated by the radiologist using the GP atlas to estimate chronological age, were compared.

In all the three tests, a paired-samples t-test was applied and the p-value was calculated to show the mean difference of the system estimated BA and the radiologist reading against the chronological age.

All results (Tables 6.1 – 6.4) show that the bone age estimated by the system is the closest to the chronological age in various age ranges, and for both female and male. Figures 6.2 - 6.12 show that our system can estimate bone age with a very high degree of accuracy. The results from the evaluation indicate that the system estimated bone age is very close to the chronological age. Moreover, the radiologist readings vary for different samples and there are also significant differences in certain categories in Test 1 (Asian and African/American).

On the whole, however, our system produces results which are accurate - the mean age difference between PA and CA is 0.05233 years. This compares well with other systems such as BoneXpert (Thodberg, 2009) which reported on error rate of 0.71 years. Our system’s accuracy is expected to improve, further. Table 6.5 shows a comparison of the accuracy between our system and a few other automated BAA systems. The result of system evaluation is encouraging and indicates the usefulness of our new method.

Table 6.5: Comparison of accuracy (error rate) between our system and other BAA systems

Comparison of error rate in years						
Mansourvar (2012)	Fischer et al., (2011)	Spampinato et al. (2010)	Thodberg, . (2009).	Rucci et al. (1995)	Hill and Pynsent (1994)	Pietka et al., 1991
Error rate is of about 0.05233 years	Error rate is of about 0.99 years	Error rate is of about 0.46 ± 0.37 years	0.71–0.72 years	Error rate is about 0.7 years	Error rate is about 0.5 years.	Error rate is roughly 1 year.

6.3 Evaluation of BAA2 subsystem

The evaluation of the BAA2 subsystem includes two sections for testing the performance of the bone age assessment system based on the clavicle images. In this test the sample data is divided into two sections based on the direction of the clavicle - right or left. The estimated bone age generated by the BAA2 subsystem is compared with the chronological age of the matching samples. The mean difference of system estimated bone age versus chronological age (CA) is then computed by a paired t-test.

6.3.1 Plots

In this test, the estimated bone age is not compared with the estimation by any radiologist. That is because none of the radiologists in UMMC has any experience in using the clavicle bone for estimating bone age. Hence, the results of subsystem BAA2 are only compared with the chronological age (CA) of the sample data. Figures 6.13- 6.14 present the results for the two categories.

Results from the BAA2 evaluation with direction separated.

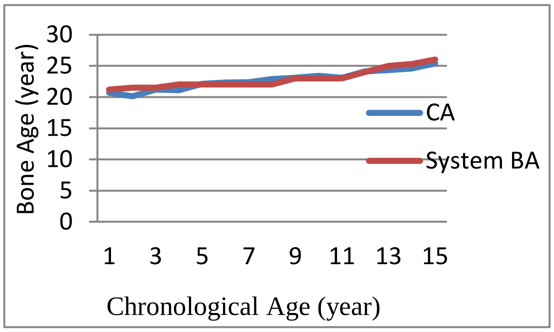

Figure 6.13: Comparison between CA and System BA of right clavicle

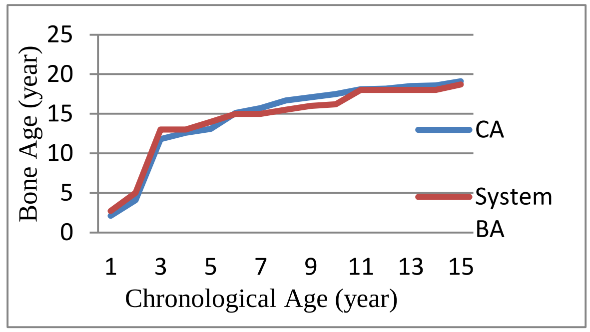

Figure 6.14: Comparison between CA and System BA of left clavicle

6.3.2 Statistical analysis

In testing the BAA2 subsystem, a paired-samples t-test was applied and the p-value was calculated to show the mean difference of the system estimated bone age against the chronological age. Table 6.5 shows the mean value and standard deviation (SD) of the paired sample t-test. The number with an asterisk indicates that the difference is significant at p-value < .05.

Table 6.6: The difference of mean chronological age and system estimated BA for BAA2 Subsystem

Test BAA2	**CA versus System BA**				
	Mean (CA)	Mean (BA)	$A_{Difference}$ = $CA_{mean} - BA_{mean}$	Standard Deviation, μ, of $A_{Difference}$	***p*- Value**
Right	22.7220	22.9000	-0.178000	0.60892	**0.277**
Left	14.5533	14.4067	0.14667	0.79809	**0.488**

* P-value < .05, significant difference

The results in Table 6.6 shows that the system estimated bone age based on analysis of the clavicle images is close to the chronological age (CA) with the mean difference of 0.178000 years for right clavicle samples and 0.14667 year for left clavicle samples.

Figure 6.13 and Figure 6.14 show that our system is able to assess the bone age very accurately for both right and left clavicles. There is no major discrepancy for both groups as the P-value of 0.277 for right clavicle and 0.488 for left clavicle. The results of the test of the BAA2 subsystem shown in Table 6.6 show that our system can give accurate estimation of bone age using the clavicle images.

6.3.3 Summary of BAA2 evaluation

The BAA2 subsystem was designed to assess bone age based on the clavicle image. Our system takes into consideration the problem of BAA of people with hand defects and those with growth abnormalities of the hand using images the clavicle bone rather than the hand-wrist bone. The BAA2 subsystem was evaluated with two cycles of data. The samples were divided into two parts: right and left clavicle images. For each group, the estimated bone age provided by the system is compared to the chronological age.

The knowledge base of the BAA2 subsystem includes 399 images in the PACS system in University of Malaya Medical Centre (UMMC). The number of images in the PACS system is rather limited as it was set up only two years ago. Although the knowledge base of BAA2 subsystem is limited, the results of the evaluation indicate that this system is a reliable method for bone age assessment with on error rate of 0.178000 years.

Future research should focus on improving the system to estimate the bone age of people of various range of age with more accuracy. By expanding the images in the knowledge base, the system also will give more accurate estimation of bone age.

6.4 User evaluation

The feedback from users is important to fine-tune the system to ensure that it meets all the requirements of the end-users. The user evaluation will give an indication on the usability of on the system and level of customer satisfaction. Bangor et al., (2008) defined usability as a series of attributes that involve the needed effort to use and the individual feeling of the user when working with the system.

The attributes for user evaluation in this study follow a well-known and accepted evaluation model - Software Usability Measurement Inventory (SUMI), that is used to determine overall judgment on usability (Kirakowski & Corbett, 1988), as follows:

- **Affect:** This term shows the emotional feelings of users (Oulanov & Pajarillo, 2001).

- **Efficiency:** This term refers to how the user shows his/her feeling about productivity, and achieving the goals (Oulanov & Pajarillo, 2001).
- **Helpfulness:** This term shows the user's perceptions about the help facilities and self-explanatory feature of the system (Kirakowski & Corbett, 1988).
- **Control:** This term refers to the degree of user’s feeling about controlling of the software when working on it (Kirakowski & Corbett, 1988).
- **Learnability:** This term shows to what degree the user can learn and also use the system (Kirakowski & Corbett, 1988).

The above attributes are incorporated into questions in the survey questionnaire regarding system usability (Refer to Appendix E).

6.4.1 Respondents

Seven persons participated in the user evaluation of the BAASHC system. Four respondents were from UMMC comprising the medical specialists and radiologists. They were the volunteers who participated in the survey and the interviews. The remaining three respondents were from the Forensic Research group from the Faculty of Computer Science and Information Technology (FCSIT), University of Malaya. Nielsen (2000) stated that five participants should be enough for the usability test because similar results will be obtained even more than six participants.

The usability testing of BAASHC was conducted on the agreed date and time and on a one-to-one basis, and hold separately in the respective office of the participants. The researcher initially briefed the participants about the system and its functions. The respondents then completed the questionnaire after they have used the BAASHC system. The participants took about five minutes to fill up the questionnaire.

The survey consists of two parts. The first part is aimed at eliciting general information while the second section is concerned about the usability issues. The questions are answered using a 5-point Likert- like scale ranging from 1= Strongly Disagree to 5= Strongly Agree. One open-ended question is included at the end of the questionnaire to solicit any additional comments from the user for improving the BAASHC system.

6.4.2 Results of usability evaluation

The user evaluation of the system was carried out over 12 days during the month of September, 2013, with the seven participants, mentioned above. The results of the usability evaluation are shown in Table 6.7.

Table 6.7: Results of Usability Evaluation of BAASHC (N=7)

No.	Statements						
	Affect	1=Strongly Disagree ⟷ 5=Strongly Agree					Mean Score
A1	Working with this system is satisfying	0%(0)	0%(0)	0%(0)	42.9%(3)	57.1%(4)	4.5714
A2	I would recommend this system for BAA to my colleagues	0%(0)	0%(0)	0%(0)	71.4%(5)	28.6%(2)	4.2857
A3	I enjoyed my sessions with this system	0%(0)	0%(0)	0%(0)	28.6%(2)	71.4%(5)	4.7143
A4 (N)	Sometimes I don’t understand the way the system behaves.	42.9%(3)	57.1%(4)	0%(0)	0%(0)	0%(0)	1.5714
A4 (R)	**The reverse of item A4 (N) **	0%(0)	0%(0)	0%(0)	57.1%(4)	42.9%(3)	4.4286
		Average score for Affect					**4.5**
	Efficiency	Strongly Disagree ⟷ Strongly Agree					Mean

B1	The automated BAA system helped me to overcome the problems that I have with the manual BAA method	0%(0)	0%(0)	0%(0)	28.6%((2)	71.4% (5)	4.7142 86
B2	Using this system saves time	0%(0)	0%(0)	0%(0)	28.6%(2)	71.4%(5)	4.7143
B3	Using this system saves manpower	0%(0)	0%(0)	0%(0)	42.9%(3)	57.1%(4)	4.5714
B4	The system is presented attractively	0%(0)	0%(0)	0%(0)	57.1%(4)	42.9%(3)	4.4286
		Average score for Efficiency					**4.6071**
	Helpfulness	Strongly Disagree ⟷ Strongly Agree					Mean
C1	Using the hand and clavicle bones is helpful in bone age assessment	0%(0)	0%(0)	0%(0)	71.4%(5)	28.6%(2)	4.2857
C2	I can work with the automated system for BAA	0%(0)	0%(0)	0%(0)	42.9%(3)	57.1%(4)	4.5714
		Average score for Helpfulness					**4.2857**
	Control	Strongly Disagree ⟷ Strongly Agree					Mean
D1	It is easy to work with the system even with a non-specialist person.	0%(0)	0%(0)	0%(0)	28.6%(2)	71.4%(5)	4.7143
D2 (N)	The system is inconsistent	14.3%(1)	71.4%(5)	14.3%(1)	0%(0)	0%(0)	2.0000
D2 (R)	**The reverse of item D2 (N) **	0%(0)	0%(0)	14.3% (1)	71.4%(5)	14.3%(1)	4.0000
D4	The speed of the system is appropriate	0%(0)	0%(0)	14.3%(1)	71.4%(5)	14.3%(1)	4.0000
D4	I can understand at a glance what are the options available in each menu.	0%(0)	0%(0)	0%(0)	71.4%(5)	28.6%(2)	4.2857
		Average score for Control					**4.25**
	Learnability	Strongly Disagree ⟷ Strongly Agree					Mean

E1 (N)	It takes too long to learn the functions of the system	28.6% (2)	71.4%(5)	0%(0)	0%(0)	0%(0)	1.7143
E1 (R)	**The reverse of item E1 (N) **	0%(0)	0%(0)	0%(0)	71.4%(5)	28.6%(2)	4.2857
E2	It is easy to make the BAA system do what I want	0%(0)	0%(0)	14.3%(1)	28.6%(2)	57.1%(4)	4.4286
E3	Overall, the system is useful for BAA	0%(0)	0%(0)	0%(0)	28.6%(2)	71.4%(5)	4.4286
E4	I can easily remember how the BAA system work	0%(0)	0%(0)	0%(0)	42.9%(3)	57.1%(4)	4.5714
		Average score for Learnability					**4.4292**

The results in Table 6.7 indicate that all the attributes in the user evaluation achieved a score above 3.0, except for the negative statement (A4, D2, and E1) of the affect, control, and learnability attribute. The negative questions in the survey are a check-and-balance way to ensure a more equitable evaluation. The low values to those negative questions show that the answers of the end-users are consistent and credible. For the negative questions, the value of the response is reversed before it is involved in calculating the mean of the relevant SUMI dimension. For example, if the respondent gives a score of 1, that value will be reversed to 5, and if the given score is 2 it will be reversed to 4.

Overall, the results of the usability evaluation are encouraging and are a good indication that the users are satisfied with our system. Table 6.8 shows the mean score for each evaluation attribute and the global mean score for the whole system.

Table 6.8: Global Mean Score and mean score for each evaluation attitude of the BAASHC system

Attributes	Global	Affect	Efficiency	Helpfulness	Control	Learnability
Mean	**4.4147**	**4.5**	**4.6071**	**4.2857**	**4.25**	**4.4292**

The usability of the BAASHC system is tested using the SUMI scale and under the subscales for Affect, Efficiency, Helpfulness, Control and Learnability. The global mean score of 4.4147 in Table 6.8 shows the highly satisfied users of the BAASHC system. The mean score for the negative questions is calculated after it has been reversed to contribute to the calculation of the summed mean score of each dimension.

It can be concluded that the system is acceptable, and it has succeeded in fulfilling the requirements of the end-users.

None of the participants answered the open-ended question soliciting their comments on improving the system.

6.5 Summary and conclusions

This chapter is divided into two main sections. In the first section the BAASHC system was evaluated through the accuracy of both subsystems and in the second section, it was evaluated by potential end-users. The results of the evaluation indicate that this system is a reliable and highly accurate automated method for bone age assessment. We contend that the accuracy of our system can be improved by comparison with some previous systems. The evaluation results also confirmed that the accuracy in bone age estimation by our proposed system is definitely an improvement in bone age assessment techniques, when compared with other BAA systems.

The user evaluation was also aimed at assessing the users’ perception of the system usability. The SUMI questionnaire was selected for system evaluation. It can be deduced from the evaluation findings that users are satisfied with the usability of system with a global mean score of 4.4147and SUMI subscale values of above 3.0. This is a cogent indication that the BAASHC system is good approach for bone age assessment.

Chapter 7: Conclusion

7.1 Introduction

This chapter concludes the research on developing an automated method for bone age assessment using X-ray images of the hand and clavicle bones. The researcher summarizes the initial objectives of the thesis and discuss to what extent this study has been able to achieve the objectives. This chapter also discusses the research approach and how it has contributed to the design of the system, called BAASHC. This study has accomplished all the goals and objectives of the research, and has fully answered the research questions. The results are discussed in the following section. This study has its limitations, but the researcher will suggest future direction for this research and how some of the limitations can be addressed.

7.2 Conclusion and discussion

This thesis has three main objectives:

i. To identify the factors that can affect assessment of bone age;
ii. To develop an automated system for bone age assessment based on the X-ray images of the hand and clavicle bones;
iii. To evaluate the accuracy and usability of the proposed bone age assessment system.

This study aims to identify the factors that can affect assessment of bone age. This was the first step in this research on development of an automated method for bone age assessment. As the project progressed, we encountered difficulties at the early stage of research, because we had to gather all the required information for this research only from the medical institutions or related facilities.

In this research, the author conducted a comprehensive documents review pertaining to various aspects of BAA, such as the history, the need for BAA methods, factors affecting BAA, and current trends in the development of a computerized or automated system for BAA.

An observational study was carried out in the X-ray lab of the Department of Biomedical Imaging, UMMC to observe the radiologists' behaviour in bone age assessment and to identify the problems they face when using the GP method as the popularly-used method for BAA among the doctors and radiologists. During the research, we realized that fulfilling the objectives was not easy as many problems were encountered in data collection. The findings from the survey discussed in Chapter 4, revealed that the main factors which contribute to automated method for assessment of bone age in the medical environment, and identified the variability such as race and gender that should be considered in the development of BAA system. The requirements for the development of our system have been identified through interviews with medical specialists, and doctors from UMMC. This initial step in data collection led to the achievement of the first objective of this research.

As a result, a web-based system for bone age assessment using hand and clavicle X-ray images, BAASHC, was developed. The results of system evaluation reveal that our system has fulfilled all the objectives. The accuracy of our system can be compared with other automated BAA systems. Table 6.4 in Chapter 6 shows the importance of improving the accuracy of bone age assessment.

The SUMI-based questionnaire (Appendix E) was used to obtain potential users feedback to the research question “How will an automated system for BAA benefit the radiologists or forensic experts?”. The global mean score of 4.4147 in Table 6.8 shows the high level of user satisfaction pertaining to the attributes - affect, efficiency, helpfulness, control, and learnability for bone age assessment. Figure 7.1 shows the comparison between the use of an automated system and the manual approach for bone age assessment (BAA) which clearly shows the benefits of using an automated BAA system.

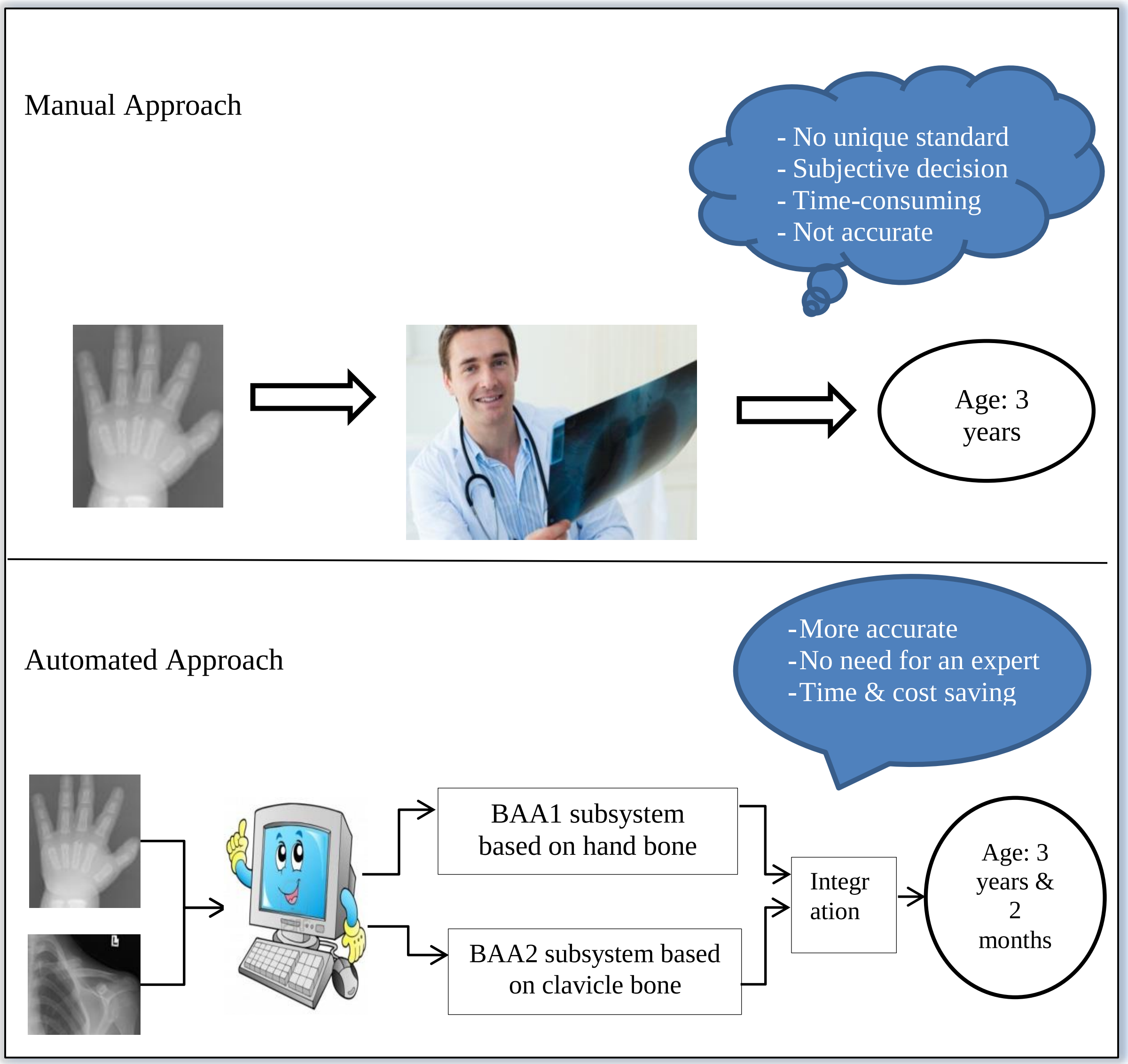

Figure 7.1: Comparison between the uses of an automated system and the manual approach for BAA

As mentioned in Section 4.2.5, the findings of the questionnaire survey, discussed in Chapter 4, have provided the answers to research questions one and two. This survey aims to identify the variability that need to be considered in developing an automated BAA system, and also the factors which can affect an automated bone age assessment system.

Research question three has been addressed in Chapter 5. This chapter highlighted the features of a new method for BAA. The implementation of BAASHC has indeed overcome the limitations of other BAA systems.

7.3 Contribution

The two main disadvantages of using the GP method as the preferred method for BAA in UMMC is that it is time-consuming and the estimation of the bone age is subjective. The need to address these drawbacks has provided the motivation to undertake this research, with the aim of developing more objective and more efficient method for bone age assessment (BAA). An automated method for bone age assessment will help the doctors and radiologists to make more accurate estimation of bone age. The system proposed in this research is an important step forward in the development of an automated bone age assessment system, that gives more accurate estimation of bone age that is very close to the chronological age.

Our system does not need a radiologist to conduct BAA, and the whole process of conducting BAA is fully automated. BAASHC has been designed as a web-based application in order to make it publicly accessible for use from anywhere, as long as there is internet connection.

The contribution of this study in the field of automated BAA system has been the development of a new approach for BAA using the new technique for the image processing stage. Unlike other BAA systems, our technique involves generating histograms instead of extracting region of interests (ROIs) in the hand bone image. The main advantage of using histogram, is that it gives high accuracy in image retrieval from large image database. In addition, our technique also involves the use of clavicle image beside the hand-wrist images, for assessment of bone age. Our BAA system, therefore, overcomes the problem of inaccuracy in BAA involving people who have defects on their hands resulting from unexpected incidents, injuries or even growth abnormalities.

Our BAA system, BAASHC, is a new automated system in view of the new approach to sample design, image preprocessing, image processing, image comparison, image retrieval, and decision-making for estimation of bone age.

The BAA system has been evaluated, scientifically. Statistical analysis had been used in the system evaluation stage to give more validity to the findings. BAASHC is very easy to implement in the web environment as an application for clinical and forensic purposes. There is minimal amount of training required to use our system. It is also a cost-saving tool, as no clinical experts are needed to use the system. Furthermore, it saves a lot of time for radiologist handling bone age assessment cases as the results are obtained within minutes.

There is no observation variability in our proposed BAA system as it is fully automated. This compares with the observation variability in the manual approach, which is 95% for confidence limits (Spampinato et al., 2010). Furthermore, our system achieves very high accuracy in bone age assessment. The mean error rate is 0.05233 years for the BAA1 subsystem, and 0.03133 years for the BAA2 subsystem. The accuracy of the estimated age produced by our BAA1 subsystem compares very favourably with systems proposed by Fischer et al. (2011), Spampinato et al. (2010), Thodberg (2009), Rucci et al. (1995), Hill and Pynsent (1994) and Pietka et al. (1991). This shows that our BAA system has considerably improved the accuracy in estimation of bone age, as compared to the other systems. This attribute makes the BAASHC a reliable method for BAA.

7.4 System limitations and future work

Table 6.1 and 6.2 in Chapter 6 show that our system does not provide high accuracy in bone age for Caucasian and Hispanic male groups. For these two groups, the radiologist reading which used the GP atlas for estimation of bone age gives more accurate results. Figure 6.7 and Figure 6.9 shows the difference between CA of sample with system BA especially in the age range of 12 to 14 years for Caucasians and 16 to 18 years for Hispanics. Despite these factors, the radiologist is still able to make reasonably accurate estimation of bone age.

The limitation of the study is partly caused by the improper distribution of X-ray images of various ranges of ages kept in the repository. Any future work in this research should be aimed at improving the accuracy in bone age assessment of these two racial groups.

Another limitation is the assessment of bone age using images of the clavicle. The samples available covers only the limited range of ages of the people. The knowledge base of the BAA2 subsystem contains 399 X-ray images which were collected since 2010, by the Picture Archiving and Communication System (PACS), Faculty of Medicine, UM. Future work should involve more images of the clavicle bone from wider range of ages.

The automated BAASHC system provides accurate estimation of bone age with results in lower error rate for the different races. By using histograms instead of extraction of ROIs, our system gives more accurate bone age assessment. The advantages of our system are that it is easy to use BAA, it saves time, and is a cost-effective approach in clinical practices.

In 2012, the initial version of BAASHC was registered as patent with patent number PI2012700291. We are in the process of establishing a commercial value for its application in the medical institutions and in crime investigation facilities or for forensic investigation. The implementation of this system would involve the integration the BAA system with the

PACS system in hospitals or similar systems in the various centres. This means that the X-ray images of the hand and the clavicle would be assessed by BAASCH and the results would be stored in PACS to be used for future reference by radiologists and doctors.

7.5 Summary

Bone age assessment (BAA) is important for monitoring endocrine disorders and for evaluation of growth in children or young adults. It is usually conducted by using the GP atlas in the medical environment and in crime and forensic investigation centres. This method of BAA using the GP atlas is time-consuming and subjected to observation variability. This has been the main motivation for developing an automated system for bone age assessment. The research has addressed the problems encountered in the use of the manual approaches for BAA. We have proposed an automated system for assessment of bone age using the hand and clavicle bones. The results of the evaluation confirmed the system to be accurate for estimating bone age.

In conclusion, this study has succeeded in fulfilling the research objectives, mentioned in Chapter 1. The outcome of the research represents an important step forward, not only in advancing automated solutions for bone age assessment but also in constantly exploring better ways of improving accuracy in bone age estimation, and improving the techniques of image processing to derive more accurate assessment results based on the images.

References

Abbey, C. K., & Barrett, H. H. (2001). Human-and model-observer performance in ramp-spectrum noise: effects of regularization and object variability. *JOSA A*, *18*(3), 473-488.

Albanese, A., Hall, C., & Stanhope, R. (1995). The use of a computerized method of bone age assessment in clinical practice. *Hormone Research in Paediatrics*, *44*(Suppl. 3), 2-7.

Allen, W. C. (2006). Overview and evolution of the ADDIE training system. *Advances in Developing Human Resources*, *8*(4), 430-441.

Arjunan, R. V., & Kumar, V. V. (2009, October). Image Classification in CBIR systems with color histogram features. In *Advances in Recent Technologies in Communication and Computing, 2009. ARTCom'09. International Conference on* (pp. 593-595). IEEE.

Baldwin-Edwards, M. (1997). The emerging European immigration regime: some reflections on implications for Southern Europe. JCMS: Journal of Common Market Studies, 35(4), 497-519.

Bangor, A., Kortum, P. T., & Miller, J. T. (2008). An empirical evaluation of the system usability scale. Intl. Journal of Human–Computer Interaction, 24(6), 574-594.

Beizer, B. (1984). *Software system testing and quality assurance*. Van Nostrand Reinhold Co.

Berst, M. J., Dolan, L., Bogdanowicz, M. M., Stevens, M. A., Chow, S., & Brandser, E. A. (2001). Effect of knowledge of chronologic age on the variability of pediatric bone age determined using the Greulich and Pyle standards. *American Journal of Roentgenology*, *176*(2), 507-510.

Bilgili, Y., Hizel, S., Kara, S. A., Sanli, C., Erdal, H. H., & Altinok, D. (2003). Accuracy of skeletal age assessment in children from birth to 6 years of age with the ultrasonographic version of the Greulich-Pyle atlas. Journal of ultrasound in medicine, 22(7), 683-690.

Black, S., Aggrawal, A., & Payne-James, J. (Eds.). (2011). *Age Estimation in the Living: The Practitioner's Guide*. John Wiley & Sons.

Black, S., & Scheuer, L. (1996). Age changes in the clavicle: from the early neonatal period to skeletal maturity. International Journal of Osteoarchaeology, 6(5), 425-434.

Bocchi, L., Ferrara, F., Nicoletti, I., & Valli, G. (2003, September). An artificial neural network architecture for skeletal age assessment. In Image Processing, 2003. ICIP 2003. Proceedings. 2003 International Conference on (Vol. 1, pp. I-1077). IEEE.

Brothwell, D. R. (1981). Digging up bones: the excavation, treatment, and study of human skeletal remains. Cornell University Press.

Bruzek, J. (2002). A method for visual determination of sex, using the human hip bone. *American Journal of Physical Anthropology, 117*(2), 157-168.

Buckler, J. M. (1983). How to make the most of bone ages. Archives of disease in childhood, 58(10), 761.

Castriota-Scanderbeg, A., Sacco, M. C., Emberti-Gialloreti, L., & Fraracci, L. (1998). Skeletal age assessment in children and young adults: comparison between a newly developed sonographic method and conventional methods. *Skeletal radiology*, *27*(5), 271-277.

Callewaert, F., Boonen, S., & Vanderschueren, D. (2010). Sex steroids and the male skeleton: a tale of two hormones. *Trends in Endocrinology & Metabolism*, *21*(2), 89-95.

Cameriere, R., Ferrante, L., Mirtella, D., & Cingolani, M. (2006). Carpals and epiphyses of radius and ulna as age indicators. *International journal of legal medicine*, *120*(3), 143-146.

Cavalli-Sforza, L. L. L., Menozzi, P., & Piazza, A. (1994). The history and geography of human genes. Princeton university press.

Cipriani, D. (2005), *South Asia and the Minimum Age of Criminal Responsibility: Raising the Standard of Protection for Children"s Rights,* UNICEF Regional Office for South Asia, Kathmandu, Nepal.

Codd, E. F. (1970). A relational model of data for large shared data banks. *Communications of the ACM, 13*(6), 377-387.

Coqueugniot, H., & Weaver, T. D. (2007). Brief communication: infracranial maturation in the skeletal collection from Coimbra, Portugal: new aging standards for epiphyseal union. American journal of physical anthropology, 134(3), 424-437.

Cox, L. A. (1996). Tanner-Whitehouse method of assessing skeletal maturity: problems and common errors. Hormone Research in Paediatrics, 45(Suppl. 2), 53-55.

Cox, L. A. (1994). Preliminary report on the validation of a grammar-based computer system for assessing skeletal maturity with the Tanner-Whitehouse 2 method. Acta Paediatrica, 83(s406), 84-85.

Crawley, H. (2007) *"When is a child not a child? Asylum, age disputes, and the process of age assessment,"* Immigration Law Practitioners" Association (ILPA), London.

David, A., Hwa, V., Metherell, L. A., Netchine, I., Camacho-Hübner, C., Clark, A. J., et al., (2011). Evidence for a continuum of genetic, phenotypic, and biochemical abnormalities in children with growth hormone insensitivity. *Endocrine reviews*, *32*(4), 472-497.

Defra 2004.The Justification of Practices Involving Ionising Radiation Regulations 2004 (SI2004 No 1769).Department for Environment, Food and Rural Affairs.

Deserno, T. M., Antani, S., & Long, R. (2009). Ontology of gaps in content-based image retrieval. *Journal of digital imaging, 22*(2), 202-215.

Diméglio, A., Charles, Y. P., Daures, J. P., De Rosa, V., & Kaboré, B. (2005). Accuracy of the Sauvegrain method in determining skeletal age during puberty. *The Journal of Bone & Joint Surgery*, *87*(8), 1689-1696.

Dünkel, F., van Kalmthout, A. M., & Schüler-Springorum, H. (Eds.). (1997). Entwicklungstendenzen und Reformstrategien im Jugendstrafrecht im europčaischen Vergleich. Forum Verlag Godesberg.

Fischer, B., Welter, P., Günther, R. W., & Deserno, T. M. (2012). Web-based bone age assessment by content-based image retrieval for case-based reasoning. International journal of computer assisted radiology and surgery, 7(3), 389-399.

Franklin, D. (2010). Forensic age estimation in human skeletal remains: current concepts and future directions. Legal Medicine, 12(1), 1-7.

Frisch, H., Riedl, S., & Waldhor, T. (1996). Computer-aided estimation of skeletal age and comparison with bone age evaluations by the method of Greulich-Pyle and Tanner-Whitehouse. Pediatric radiology, 26(3), 226-231.

Flecker, H. (1932). Roentgenographic observations of the times of appearance of epiphyses and their fusion with the diaphyses. Journal of anatomy, 67(Pt 1), 118.

Fleshman, K. (2000). Bone age determination in a paediatric population as an indicator of nutritional status. Tropical doctor, 30(1), 16-18.

Garamendi, P. M., Landa, M. I., Ballesteros, J., & Solano, M. A. (2005). Reliability of the methods applied to assess age minority in living subjects around 18 years old: A survey on a Moroccan origin population. Forensic science international, 154(1), 3-12.

Garn, S. M., Keith, P., Poznanski, A. K., & Nagy, J. M. (1972). Metacarpophalangeal length in the evaluation of skeletal malformation. Radiology, 105(2), 375-381.

Giordano, D., Spampinato, C., Scarciofalo, G., & Leonardi, R. (2010). An automatic system for skeletal bone age measurement by robust processing of carpal and piphysial/metaphysial bones. Instrumentation and Measurement, IEEE Transactions on, 59(10), 2539-2553.

Giordano, D., Faro, A., Spampinato, C., & Leonardi, R. (2011, June). A learning tool for assessing skeletal bone age in radiology. In Computer-Based Medical Systems (CBMS), 2011 24th International Symposium on (pp. 1-6). IEEE.

Gilsanz, V., & Ratib, O. (2005). Hand bone age: a digital atlas of skeletal maturity. Springer.

Greulich, W. W., & Pyle, S. I. (1959). Radiographic atlas of skeletal development of the hand and wrist. The American Journal of the Medical Sciences, 238(3), 393.

Goldberg, D. J., Dodds, K., Avitabile, C. M., Glatz, A. C., Brodsky, J. L., Semeao, E. J., et. Al., (2012). Children With Protein-Losing Enteropathy After the Fontan Operation Are at Risk for Abnormal Bone Mineral Density. Pediatric cardiology, 33(8), 1264-1268.

Graham, C. B. (1972). Assessment of bone maturation--methods and pitfalls. Radiologic Clinics of North America, 10(2), 185.

Greenspan, F. S., & Gardner, D. G. (Eds.). (1997). Basic & clinical endocrinology (Vol. 5). Stamford, CT: Appleton & Lange.

Gross, G. W., Boone, J. M., & Bishop, D. M. (1995). Pediatric skeletal age: determination with neural networks. Radiology, 195(3), 689-695.

Gudivada, V. N., & Raghavan, V. V. (1995). Content based image retrieval systems. Computer, 28(9), 18-22.

Hill, K., & Pynsent, P. B. (1994). A fully automated bone-ageing system. *Acta Paediatrica*, *83*(s406), 81-83.

Hsieh, C. W., Jong, T. L., & Tiu, C. M. (2007). Bone age estimation based on phalanx information with fuzzy constrain of carpals. Medical & biological engineering & computing, 45(3), 283-295.

Hsieh, C. W., Jong, T. L., Chou, Y. H., & Tiu, C. M. (2007). Follow us. *Chinese medical journal*, *120*(9), 767-770.

Hsieh, C. W., Jong, T. L., Chou, Y. H., & Tiu, C. M. (2007). "Computerized geometric features of carpal bone for bone age estimation." CHINESE MEDICAL JOURNAL-BEIJING-ENGLISH EDITION- 120(9): 767.

Johnston, F. E. (2002). Social and economic influences on growth and secular trends. Human growth and development. San Diego, CA: Academic Press. p, 197-212.

Johnston, F. E., & Jahina, S. B. (1965). The contribution of the carpal bones to the assessment of skeletal age. *American Journal of Physical Anthropology, 23*(4), 349-354.

Judge, T. A., Bono, J. E., Ilies, R., & Gerhardt, M. W. (2002). Personality and leadership: a qualitative and quantitative review. *Journal of applied psychology, 87*(4), 765.

Kaplan S. (1990) Growth and growth hormone: disorders of the anterior pituitary. In: Kaplan SA Clinical Pediatric Endocrinology. (2nd ed.) Philadelphia: W.B.Saunders Company,pgs. 1–62.

Kaplan. S, Clinical Pediatric and Adolescent Endocrinology, W.B. Saunders,Philadelphia, 1982.

Kearns, G. S., & Lederer, A. L. (2004). The impact of industry contextual factors on IT focus and the use of IT for competitive advantage. Information & Management, 41(7), 899-919.

King, D. G., Steventon, D. M., O'Sullivan, M. P., Cook, A. M., Hornsby, V. P. L., Jefferson, I. G., & King, P. R. (1994). Reproducibility of bone ages when performed by radiology registrars: an audit of Tanner and Whitehouse II versus Greulich and Pyle methods. British journal of radiology, 67(801), 848-851.

Kirakowski, J. and Corbett, M. (1988). Measuring User Satisfaction. In Jones, D. M. and Winder, R. (ed), People and Computers. Cambridge: Cambridge University Press.

Konstantinidis, K., Gasteratos, A., & Andreadis, I. (2005). Image retrieval based on fuzzy color histogram processing. Optics Communications, 248(4), 375-386.

Kreitner, K. F., Schweden, F. J., Riepert, T., Nafe, B., & Thelen, M. (1998). Bone age determination based on the study of the medial extremity of the clavicle. European radiology, 8(7), 1116-1122.

K. Sato, K. Ashizawa, M. Anzo, F. Otsuki, S. Kaneko, T. Tanaka, K. Tsukagoshi, A. Nimura, H. Matsuok, N. Matsuo, H. Mitani, and M. Murata, "Setting up an automated system for evaluation of bone age," *Endocrine Journal*, vol. 46, pp.S97–100, 1999.

Kwabwe, S. A., PAL, S. K., & King, R. A. (1985). Recognition of bones from X-rays of the hand†. International journal of systems science, 16(4), 403-413.

Langley-Shirley, N., & Jantz, R. L. (2010). A Bayesian Approach to Age Estimation in Modern Americans from the Clavicle*. Journal of forensic sciences, 55(3), 571-583.

Lei, Z., Fuzong, L., & Bo, Z. (1999). A CBIR method based on color-spatial feature. In TENCON 99. Proceedings of the IEEE Region 10 Conference (Vol. 1, pp. 166-169). IEEE.

Leite, H. R., O'Reilly, M. T., & Close, J. M. (1987). Skeletal age assessment using the first, second, and third fingers of the hand. American Journal of Orthodontics and Dentofacial Orthopedics, 92(6), 492-498.

Lewis, M. W. (1998). Iterative triangulation: a theory development process using existing case studies. Journal of Operations Management, 16(4), 455-469.

Liu, J., Qi, J., Liu, Z., Ning, Q., & Luo, X. (2008). Automatic bone age assessment based on intelligent algorithms and comparison with TW3 method. Computerized Medical Imaging and Graphics, 32(8), 678-684.

Liu, G. H., & Yang, J. Y. (2013). Content-based image retrieval using color difference histogram. Pattern Recognition, 46(1), 188-198.

Liversidge, H. M., Lyons, F. & Hector, M. P. 2003. The accuracy of three methods of age estimation using radiographic measurements of developing teeth. *Forensic Science International*, 131**,** 22-29.

Lucina. S, M.R. Hackman, *Age Estimation in the Living: a test of 6 radiographic methods*, PhD thesis, University of Dundee,2012.

Luis-Garcia, D., Martín-Fernández, M., Arribas, J. I., & Alberola-López, C. (2003, September). A fully automatic algorithm for contour detection of bones in hand radiographs using active contours. In Image Processing, 2003. ICIP 2003. Proceedings. 2003 International Conference on (Vol. 3, pp. III-421). IEEE.

Mackenzie, N., & Knipe, S. (2006). Research dilemmas: Paradigms, methods and methodology. Issues in educational research, 16(2), 193-205.

Mackay, D. H. (1952). Skeletal maturation in the hand A study of development in East African children. Transactions of the Royal Society of Tropical Medicine and Hygiene, 46(2), 135-IN20.

Mahmoodi. S, B. S. Sharif, E. G. Chester, J. P. Owen, and R. E. J. Lee, “Skeletal growth estimation using radiographic image processing and analysis,” *IEEE Transactions on Information Technology in Biomedicine*, vol. 4, no. 4, pp. 292–297, 2000.

Mansourvara, M., Raj, R. G., Ismail, M., Kareem, S. A., Shanmugam, S, et al. (2012). “Automated web based system for bone age assessment using histogram technique". Malaysian Journal of Computer Science 25(3): 107-121.

Mansourvar, M., Ismail, M. A., Herawan, T., Gopal Raj, R., Abdul Kareem, S., & Nasaruddin, F. H. (2013). Automated Bone Age Assessment: Motivation, Taxonomies, and Challenges. *Computational and Mathematical Methods in Medicine, 2013*.

Mansourvar, M., Ismail, M. A., Kareem, S. A., Nasaruddin, F. H., & Raj, R. G. (2014, January). A Quantitative Study for Developing a Computerized System for Bone Age Assessment in University of Malaya Medical Center. In *Proceedings of the First International Conference on Advanced Data and Information Engineering (DaEng-2013)* (pp. 659-666). Springer Singapore.

Mansourvar M, Ismail MA, Raj RG, Kareem SA, Aik S, Gunalan R, Antony CD, The Applicability of Greulich and Pyle Atlas to Assess Skeletal Age for Four Ethnic Groups, Journal of Forensic and Legal Medicine2013), doi: 10.1016/j.jflm.2013.11.011.

Marshall, W. A. (1977). Human growth and its disorders. Academic Press Inc.(London) Ltd.

McKern, T. W., & Stewart, T. D. (1957). Skeletal age changes in young American males analysed from the standpoint of age identification (No. QREC-EP-45). Quartermaster research and engineering command natick ma.

Meijer, E., & Bierman, G. (2011). A co-relational model of data for large shared data banks. *Communications of the ACM, 54*(4), 49-58.

Michael, D. J., & Nelson, A. C. (1989). HANDX: A model-based system for automatic segmentation of bones from digital hand radiographs. Medical Imaging, IEEE Transactions on, 8(1), 64-69.

Miguel A. Martin-Fernandez, Marcos Martin-Fernandez, Carlos Alberola-Lopez, Automatic bone age assessment: a registration approach‖, Medical Imaging 2003: Image Processing,Proceedings of SPIE, vol. 5032, pp. 1765-1776, 2003.

Milner, G. R., Levick, R. K., & Kay, R. (1986). Assessment of bone age: a comparison of the Greulich and Pyle, and the Tanner and Whitehouse methods. Clinical radiology, 37(2), 119-121.

Mould, R. (1995). Roentgen and the discovery of X-rays. *The British journal of radiology*, *68*(815), 1145-1176.

Müller, H., Despont-Gros, C., Hersh, W., Jensen, J., Lovis, C., & Geissbuhler, A. (2006). Health care professionals' image use and search behaviour. Proceedings of Medical Informatics Europe (MIE 2006), Maastricht, Netherlands, 24-32.

Nielsen, J. (2000) Why You Only Need to Test with 5 Users: Jakob Nielsen's Alertbox. [Online] Available at: http://www.useit.com/alertbox/20000319.html [Accessed 15th March 2008].

Niemeijer, M. (2002). Automating skeletal age assessment. Master's thesis, Utrecht University.

Ogata, S., & Uhthoff, H. K. (1990). The early development and ossification of the human clavicle-an embryologic study. Acta Orthopaedica, 61(4), 330-334.

O'Keeffe, D. Denoising of carpal bones for computerised assessment of bone age [Ph.D. thesis], University of Canterbury Christchurch, Christchurch, New Zealand, 2010.

Oulanov, A. and E. J. Pajarillo (2001). "Usability evaluation of the City University of New York CUNY+ database." Electronic Library, The 19(2): 84-92.

Patil, S. T., Parchand, M. P., Meshram, M. M., & Kamdi, N. Y. (2012). Applicability of Greulich and Pyle skeletal age standards to Indian children. Forensic Science International, 216(1), 200-e1.

Paewinsky, E., Pfeiffer, H., & Brinkmann, B. (2005). Quantification of secondary dentine formation from orthopantomograms—a contribution to forensic age estimation methods in adults. International journal of legal medicine, 119(1), 27-30.

Pearlson, K., & Saunders, C. S. (2004). Managing and using information systems: A strategic approach (Vol. 2). Hoboken, NJ: Wiley.

Peterson, C. (2003). Bringing ADDIE to life: Instructional design at its best. *Journal of Educational Multimedia and Hypermedia*, *12*(3), 227-241.

Pietka, E., McNitt-Gray, M. F., Kuo, M. L., & Huang, H. K. (1991). Computer-assisted phalangeal analysis in skeletal age assessment. Medical Imaging, IEEE Transactions on, 10(4), 616-620.

Pietka, E., Gertych, A., Pospiech, S., Cao, F., Huang, H. K., & Gilsanz, V. (2001). Computer-assisted bone age assessment: Image preprocessing and epiphyseal/metaphyseal ROI extraction. Medical Imaging, IEEE Transactions on, 20(8), 715-729.

Picum (Platform for International Cooperation n Undocumented Migrants).Los niños indocumentados en España: víctimas invisibles de las restricciones a la inmigración. PICUM. Brussels. 2008.

Pietka, E., Pospiech, S., Gertych, A., Cao, F., Huang, H. K., & Gilsanz, V. (2001). Computer automated approach to the extraction of epiphyseal regions in hand radiographs. Journal of Digital Imaging, 14(4), 165-172.

Pietka, E., A. Gertych, et al. Computer-assisted bone age assessment: Image preprocessing and epiphyseal/metaphyseal ROI extraction. IEEE Transactions on Medical Imaging 20(8), 715-729, 2001.

Pietka, E. (1995). Computer-assisted bone age assessment based on features automatically extracted from a hand radiograph. Computerized medical imaging and graphics, 19(3), 251-259.

Pratt. W. K., Digital Image Processing, John Wiley and Sons, Inc., New York, 3rd edition, 2001.

Premkumar, G., & King, W. R. (1992). An empirical assessment of information systems planning and the role of information systems in organizations. Journal of Management Information Systems, 99-125.

Pronovost, P. J., Goeschel, C. A., Colantuoni, E., Watson, S., Lubomski, L. H., Berenholtz, S. M., et. al., (2010). Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: observational study. BMJ: British Medical Journal, 340.

Poznanski, A. K., Hernandez, R. J., Guire, K. E., Bereza, U. L., & Garn, S. M. (1978). Carpal length in children--a useful measurement in the diagnosis of rheumatoid arthritis and some concenital malformation syndromes. *Radiology*, *129*(3), 661-668.

R.C. Gonzalez, R.E. Woods, Digital Image Processing, Addison-Wesley, Reading, MA, 1992.Y. Liang, H. Zhai, P. Chavel, Opt. Commun. 212 (2002) ,247.

Rosenbloom, A. L. & Tanner, J. M. 1998. Misuse of Tanner puberty stages to estimate chronological age. Pediatrics, 102, 1494.

Roche, A. F., Chumlea, W., & Thissen, D. (1988). Assessing the skeletal maturity of the hand-wrist: Fels method. Springfield: Thomas.

Roemmich J. N., R. M. Blizzard, S. D. Peddada, R. M. Malina, A. F. Roche, J. M. Tanner, and A. D. Rogol, "Longitudinal assessment of hormonal and physical alterations during normal puberty in boys. IV: Predictions of adult height by the Bayley-Pinneau, Roche-Wainer-Thissen, and Tanner-Whitehouse methods compared," *American Journal of Human Biology*, vol. 9, pp. 371–380, 1997.

Rosenbloom, A. L. (2012). Inaccuracy of age assessment from images of postpubescent subjects in cases of alleged child pornography. International journal of legal medicine, 1-5.

Rosenfeld RG, Cohen P (2002) Disorders of growth hormone / insulin-like growth factor secretion and action. In: Sperling MA, ed. Pediatric Endocrinology. Philadelphia, PA: Saunders; pgs 211–288.

Rucci, M., Coppini, G., Nicoletti, I., Cheli, D., & Valli, G. (1995). Automatic analysis of hand radiographs for the assessment of skeletal age: a subsymbolic approach. Computers and biomedical research, 28(3), 239-256.

Ruxton S. (2003), Separated Children and EU Asylum and Immigration Policy, Save the Children.

Schmeling A, Reisinger W, Geserick G, Olze A (2008). Forensic Age estimation of liveadolescents and Young Adults. En: Forensic Pathology reviews. Vol 5.Editor:MichaelTsokos. Forensic Pathology Reviews, vol 5. Humana Press. 2008.

Schmeling, A., Reisinger, W., Loreck, D., Vendura, K., Markus, W., & Geserick, G. (2000). Effects of ethnicity on skeletal maturation: consequences for forensic age estimations. International Journal of Legal Medicine, 113(5), 253-258.

Schmeling, A., Garamendi, P. M., Prieto, J. L., & Landa, M. I. (2011). Forensic age estimation in unaccompanied minors and young living adults. Forensic medicine—from old problems to new challenges. Intech, 77-120.

Schmeling, A., Reisinger, W., Geserick, G., & Olze, A. (2006). Age estimation of unaccompanied minors: part I. General considerations. Forensic science international, 159, S61-S64.

Schmeling, A., Baumann, U., Schmidt, S., Wernecke, K. D., & Reisinger, W. (2006). Reference data for the Thiemann–Nitz method of assessing skeletal age for the purpose of forensic age estimation. International journal of legal medicine, 120(1), 1-4.

Schmeling, A., Grundmann, C., Fuhrmann, A., Kaatsch, H. J., Knell, B., Ramsthaler, F., Reisinger,W., Riepert, T., Ritz-Timme, S., Rösing, F., Rötzscher, K. &Geserick, G. 2008.Criteria forage estimation in living individuals.*International Journal of Legal Medicine*, 122**,** 457-460.

Schmeling, A., Olze, A., Reisinger, W. &Geserick, G. 2005. Forensic Age Estimation and Ethnicity.*Legal Medicine*, 7**,** 134-137.

Scheuer, J. L. & Black, S. 2000a. Development and ageing of the juvenile skeleton.*In:* COX, M.& MAYS, S. (eds.) *Human Osteology. In Archaeology and Forensic Science.*Cambridge:Cambridge University Press.
Schmeling, A., Grundmann, C., Fuhrmann, A., Kaatsch, H. J., Knell, B., Ramsthaler, F., & Geserick, G. (2008). Criteria for age estimation in living individuals. International journal of legal medicine, 122(6), 457-460.

Schonlau, M., Fricker, R. D. Jr. and Elliott, M. N. (2002).Conducting research surveys via email and the Web.Santa Monica, CA : Rand.

Singh, J., & Chavali, K. H. (2011). Age estimation from clavicular epiphyseal union sequencing in a Northwest Indian population of the Chandigarh region. Journal of forensic and legal medicine, 18(2), 82-87.

Singh, P., Gorea, R. K., Oberoi, S. S., & Kapila, A. K. (2010). Age estimation from medial end of clavicle by x-ray examination.

Smith, T., & Brownlees, L. (2011). Age assessment practices: a literature review & annotated bibliography. Nova Iorque: Child Protection Section, United Nations Children's Fund, New York, 1.

Stevenson P. 1924. Age order of epiphyseal union in man. Am J Phys Anthropol 7:53-93. Steyn M, and Iscan M. 1998. Sexual dimorphism in the crania and mandibles of South African whites. Forensic Sci Int 98:9-16.

SUMI (2008). Software Usability Measurement Inventory: The de Facto Industry Standard Evaluation Questionnaire for Assessing Quality of Use of Software by End Users. [Online] Available at: http://sumi.ucc.ie/whatis.html. [Accessed 15th March 2008].

Szilvassy V. 1977. Altersschaetzung an der sternalen gelenkflaechen der schluesselbeine. Beitr Gerichtl Med 35:343-345.

Tashakkori, A. and J. W. Creswell (2007). "Editorial: The new era of mixed methods." Journal of Mixed Methods Research 1(1): 3-7.

Tanner, J. M., Whitehouse, R. H., Marshall, W. A., & Carter, B. S. (1975). Prediction of adult height from height, bone age, and occurrence of menarche, at ages 4 to 16 with allowance for midparent height. Archives of disease in childhood, 50(1), 14-26.

Tanner, J. M., & Gibbons, R. D. (1994). A computerized image analysis system for estimating Tanner-Whitehouse 2 bone age. Hormone Research in Paediatrics, 42(6), 282-287.

Tanner, J. M., R. Healy, H. Goldstein, and N. Cameron, *Assessment of skeletal maturity and prediction of adult height (TW3 method)*, WB Saunders, 3rd edition, 2001.

Tanner J. M., R. H. Whitehouse, N. Cameron, W. A. Marshall, M. J. R. Healy, and H. Goldstein, *Assessment of skeletal maturity and prediction of adult height (TW2 method)*, Academic Press, London, 2nd edition, 1983.

Todd, T. W., & D'Errico, J. (1928). The clavicular epiphyses. American Journal of Anatomy, 41(1), 25-50.

Todd, T. W. 1930. The Anatomical Features of EpiphysialUnion.*Child Development,* 1**,** 186-194.

Torroni, A., H.-J. Bandelt, et al. (2001). "A signal, from human mtDNA, of postglacial recolonization in Europe." The American Journal of Human Genetics 69(4): 844-852.

Tristan-Vega, A., & Arribas, J. I. (2008). A radius and ulna TW3 bone age assessment system. Biomedical Engineering, IEEE Transactions on, 55(5), 1463-1476.

Tristán, F. J., Ruiz, S. F., Pérez, D. L. C. A., Lobo, T. G., Aguilar, C. M., & Collado, T. F. (2007). The influence of nutrition and social environment on the bone maturation of children]. Nutrición hospitalaria: organo oficial de la Sociedad Española de Nutrición Parenteral y Enteral, 22(4), 417.

Thodberg, H. H., Kreiborg, S., Juul, A., & Pedersen, K. D. (2009). The BoneXpert method for automated determination of skeletal maturity. Medical Imaging, IEEE Transactions on, 28(1), 52-66.

Unrath, M., H. H. Thodberg, et al. (2013). "Automation of Bone Age Reading and a New Prediction Model Improve Adult Height Prediction in Children with Short Stature." Hormone research in paediatrics 78(5-6): 312-319.

Van Rijn, R. R., Lequin, M. H., & Thodberg, H. H. (2009). Automatic determination of Greulich and Pyle bone age in healthy Dutch children. Pediatric radiology, 39(6), 591-597.

Warren M. W., K. R. Smith, P. R. Stubbefield, S. S. Martin, and H. A. Walsh-Haney, “Use of radiographic atlases inmass fatality,” Journal of Forensic Sciences,vol. 45, no. 2, pp. 467–470, 2000.

Webb, P. A. O., & Suchey, J. M. (1985). Epiphyseal union of the anterior iliac crest and medial clavicle in a modern multiracial sample of American males and females. American Journal of Physical Anthropology, 68(4), 457-466.

Werther, G. A. (1996). Growth hormone measurements versus auxology in treatment decisions: the Australian experience. The Journal of pediatrics, 128(5), S47-S51.

Whitehead, H. M., Boreham, C., Mcllrath, E. M., Sheridan, B., Kennedy, L., Atkinson, A. B., & Madden, D. R. (1992). Growth hormone treatment of adults withgrowth hormone deficiency: results of a 13-month placebo controlled cross-over study. Clinical endocrinology, 36(1), 45-52.

Whittaker, J. A. (2000). What is software testing? And why is it so hard?. Software, IEEE, 17(1), 70-79.

Xie, H.-T., & Meng, X.-W. (2011). A personalized information service model adapting to user requirement evolution. *Dianzi Xuebao(Acta Electronica Sinica), 39*(3), 643-648.

Zerin, J. M., & Hernandez, R. J. (1991). Approach to skeletal maturation. Hand clinics, 7(1), 53-62.

Zhang, A., Gertych, A., Kurkowska-Pospiech, S., Liu, B. J., & Huang, H. K. (2006, March). Carpal bone analysis in bone age assessment. In *Medical Imaging* (pp. 61450Z-61450Z). International Society for Optics and Photonics.

Zhang, A.,Gertych, A., Sayre, J., Pospiech-Kurkowska, S., & Huang, H. K. (2007). Bone age assessment of children using a digital hand atlas. Computerized Medical Imaging and Graphics, 31(4), 322-331.

PhD Related Awards and Publications

Awards:

PECIPTA 2013 **(**International Conference and Exposition on Invention of Institutions of Higher Leering), Silver medal, November 2013.

ITEX 2012 (International Invention, Innovation & Technology Exhibition): Bronze Medal, 2012, (INTERNATIONAL), Ministry of Science Technology and Innovation, 2012.

Journal:

Marjan Mansourvar,Ismail, M.A, Tutut Herawan, Ram Gopal Raj, Sameem Abdul Kareem and Fariza Hanum Nasaruddin (2014), Automated bone Age Assessment: Motivation, Taxonomies and Challenges, Computational and Mathematical Methods in Medicine. (*ISI-Cited Publication*).

Marjan Mansourvar, Maizatul Akmar Ismail, Ram Gopal Raj, Sameem Abdul Kareem, Saw Aik, Roshan Gunalan, Chermaine Deepa Antony, (2013), The Applicability of Greulich and Pyle Atlas to Assess Skeletal Age for Four Ethnic Groups, Journal of Forensic and Legal Medicine. (ISI-Cited Publication).

Marjan Mansourvar, Ram Gopal Raj , Maizatul Akmar Ismail, S. Abdul-Kareem , Saravanan Shanmugam, Shahrom Wahid, Rohana Mahmud, Rukaini Abdullah , Fariza Hanum Nasaruddin, Norisma Idris , (2012) Automated Web Based System for Bone Age Assessment using Histogram Technique, pp 107-121, Malaysian Journal of Computer Science, Volume 25, No 3, 2012. (*ISI-Cited Publication*)

Marjan Mansourvar, Maizatul Akmar Ismail, Fariza Hanum Nasaruddin, (2014), Bone Age Assessment: A Review, The Malaysian Journal of Medical Sciences, (Under Review) (*SCOPUS-Cited Publication*).

Marjan Mansourvar, Maizatul Akmar Ismail, Sameem Abdul Kareem, Ram Gopal Raj, Fariza Hanum Nasaruddin, (2014), Content-Based Image Retrieval (CBIR) in Medical Systems, International Journal of Information Technology, (Under Review) (*SCOPUS-Cited Publication*).

Marjan Mansourvar, Maizatul Akmar Ismail, Sameem Abdul Kareem, Ram Gopal Raj, Fariza Hanum Nasaruddin, Saw Aik, Roshan Gunalan, Chermaine Deepa Antony, (2013), Bone Age Estimation Using Clavicle Bone, *Journal of Forensic Medicine and Toxicology*. (*SCOPUS-Cited Publication*).

Proceedings:

Mansourvar, M., Ismail, M. A., Kareem, S. A., Raj, R. G., Nassaruddin, F. H., Mahmud, R., et al., (2012, September). A Computer-Based System to Support Intelligent Forensic Study. In *Computational Intelligence, Modelling and Simulation (CIMSiM), 2012 Fourth International Conference on* (pp. 117-119). IEEE.

Marjan Mansourvar, Maizatul Akmar Ismail, Sameem Abdul Kareem, Fariza Hanum Nasaruddin, Ram Gopal Raj. (2013, December). A Quantitative Study for Developing A Computerized System for Bone Age Assessment in University of Malaya Medical Center. In International Conference on Advanced Data and Information Engineering (DaEng-2013), (Scopus/ISI index).

Mansourvar, M., Ismail, M. A., Automatic Method for Bone Age Assessment Based on Combined Method, In International Conference on Computer & Information Sciences (ICCOINS), 2014 . IEEE.

Appendix A

Observational Study

Question 1

Objective:

Demographic Study: To find out the demographic background of the respondent and her knowledge and experience level in BAA.

Question 2

Objective:

To find out the history of the BAA procedure in UMMC, and issues pertaining to its implementation such as the time and period of training the radiologists in BAA.

Question 3

Objective:

To find out how BAA is implemented in UMMC.

Question 4

Objective:

To find out the main reasons for conducting BAA in UMMC.

Question 5

Objective:

To find out the problems that radiologists faced when conducting bone age assessment in UMMC.

Question6

Objective

To find out the frequency of conducting BAA by radiologist in UMMC

Question7

Objective

To find out the significance of using BAA in UMMC

****** Thank you for your time *****

Appendix B

Questionnaire Survey

Year: 2012/2013

Dear Respondent,

I am Marjan Mansourvar, a PhD student from the Department of Information Science, Faculty of Computer Science and Information Technology, University of Malaya, under the supervision of Dr. Maizatul Akmar Ismail**.**

I would be grateful if you can spend some of your precious time to complete the questionnaire. It will take about 5 to 7 minutes of your time and all the information given will be kept confidential and will solely be used for academic purposes.

Thank you very much for your kind cooperation in advance.

Briefly, about the study:

Bone age assessment (BAA) is a useful but time-consuming process in clinical science as well as forensic science. BAA often is used to evaluate the growth status of children that might be influenced by hormonal problems and genetic disorders. The main aim of this research is to develop a new automated system for assessment of bone age using X-ray images of the hand and clavicle. An automated system will improve the accuracy of BAA and reduce cost through the reduction of the radiologist's time to conduct BAA and the elimination of the observation variability

Yours Sincerely,
Marjan Mansourvar
Department of Information Science
Faculty of Computer Science and Information Technology, University of Malaya
Marjan2012@siswa.um.edu.my

Section A

Part 1: Personal Information

1) Academic Level :

Master’s Candidate (Year of Study)

Year 1 ☐ Year 2 ☐ Year 3 ☐

PhD Candidate ☐

2) Gender :

Male ☐ Female ☐

3) Age :

19 years and below ☐

20-29 years ☐

30-39 years ☐

40-59 years ☐

Part 2: Experience Level

1) Please state your experience in Bone Age Assessment

Below 1 year ☐ 2 years to 3 years ☐

4 years to 5 years ☐ Above 5 years ☐

2) How long does it take to be an expert in assessing bone age from X-ray images?

Between 1 to 2 months ☐ Between 2 to 4 months ☐

Between 4 to 6 months ☐ Between 6 to 12 months ☐

3) Which atlas do you use for BAA :

Pyle atlas ☐

Others (Please Specify) ____________ ☐

Part 3: Evaluation of Current Method

1) How many cases approximately of bone age assessment do you handle in a month?

Between 5 and 10 cases ☐

Between 10 and 20 cases ☐

Between 20 and 30 cases ☐

More than 30 cases ☐

2) What are the main reasons for conducting BAA?

Diagnosis of growth disorders ☐

Estimation of height ☐

Control the dosage of growth hormone used in treatment ☐

To determine the age of patients who do not have documentary evidence ☐

Others (Please specify) ____________ ☐

3) Usually, how long does it take to assess the bone age when normal images are used?

Between 5 and 10 minutes ☐ Between 10 and 15 minutes ☐

Between 15 and 20 minutes ☐ Above 20 minutes ☐

4) What are the advantages for using the current atlas for BAA?

Easy to use ☐ Saves time ☐

Accurate ☐ Others (Please specify) ____________

5) What are the main problems for using Greulich & Pyle (GP) atlas in BAA?

Time-consuming ☐ Low precision ☐

Subjective decision ☐ Others (Please specify) ____________

6) What is the normal error rate in using the current method for BAA?

Between 3 and 6 months ☐ Between 6 and 12 months ☐

Between 1 and 2 years ☐ Between 2 and 3 years ☐

Between 3 and 4 years ☐ Above 4 years ☐

Part 4: Effective Factors

1) Does race have any effect on the diagnosis of bone age?

Yes ☐ No ☐

2) Does gender have effect on the diagnosis of bone age?

Yes ☐ No ☐

3) Does noisy image have any effect on the diagnosis of bone age?

Yes ☐ No ☐

Part 5: Alternative Selection

1) Do you have to handle low quality X-ray images (radiographs) of the hand (such as noisy images or incomplete samples)?

Yes ☐ No ☐

2) Do you have problems with images of low quality when conducting BAA?

Yes ☐ No ☐

3) How long does it take to assess the bone age when working with noisy images?

Less than 10 minutes ☐ Between 10 and 20 minutes ☐

Between 20 and 30 minutes ☐ Above 30 minutes ☐

4) Aside from the images of the bone of the left hand, do you have other alternatives?

Yes ☐ No ☐

4-A) If yes, please specify the bone(s) you used:

Elbow ☐ Knee ☐

Pelvic ☐ Foot ☐

Clavicle ☐ Others (Please specify) ☐

SECTION B:

The followings statements concern the significance, and motivation for designing, implementing, and developing ane automated system for bone age assessment.
Please indicate your level of agreement about each statement using the 5-point Likert-like scale. (**1 --- ‘STRONGLY DISAGREE’ and 5 --- ‘STRONGLY AGREE’)**

1) Do you agree to have a computerized system for BAA in UMMC?

1 ○ 2 ○ 3 ○ 4 ○ 5 ○

2) An automated system would help the radiologist to speed up the process of BAA.

1 ○ 2 ○ 3 ○ 4 ○ 5 ○

3) An automated system should increase the accuracy of the assessment of bone age.

1 ○ 2 ○ 3 ○ 4 ○ 5 ○

4) An automated system in BAA would help to eliminate the observation variability.

1 ○ 2 ○ 3 ○ 4 ○ 5 ○

5) An automated system based on the combined method (using hand and clavicle) would be able to overcome the problem of noisy images.

1 ○ 2 ○ 3 ○ 4 ○ 5 ○

6) An automated system to record the patients’ estimated age would increase efficiency and effectiveness in further BAA cases.

1 ○ 2 ○ 3 ○ 4 ○ 5 ○

********** Thank you very much for completing this questionnaire **********

Appendix C

Year: 2013

The Interview Questions

1- What is the main method for bone age assessment in UMMC?

2- What is the maximum and minimum error rate (difference between chronological age and estimated age)?

3- What are the main problems faced in using the current method?

4- If you do not use the left hand image, what do you use for bone age assessment?

5- Which bone do you prefer to use to assess bone age and which one produces fewer error? (Elbow, knee, clavicle, pelvic , …., etc)

6- Do you think it is essential to have an automated system for bone age assessment to replace the manual method?

7- Which BAA method do you prefer? Manual or automated?

8- Which features are important to be incorporated into a computerized BAA system?

9- Do you prefer a web-based system or stand-based system?

****** Thank you very much for your kind cooperation ******

Appendix D

Table of Coefficients for Prediction of Adult Height for Boys

Age (years)	Coefficient for Height	Coefficient for Age	Coefficient for Bone Age	Constant
4–7	1.20	–7.3	0	82
8.0	1.22	–7.2	–0.4	82
8.5	1.23	–0.7	–0.7	82
9.0	1.22	–6.8	–0.8	82
9.5	1.21	-6.5	-0.8	82
10.0	1.20	–6.2	–1.0	83
10.5	1.19	-5.9	-1.2	84
11.0	1.16	-5.5	-1.6	89
11.5	1.13	5.1	-2.0	94
12.0	1.08	-4.2	-2.6	98
12.5	1.03	-3.4	-3.2	108
13.0	0.98	-2.6	-3.8	108
13.5	0.94	-1.9	-4.4	113
14.0	0.90	-1.4	-4.5	114
14.5	0.87	-1.0	-4.6	114
15.0	0.87	-0.8	-3.8	104
15.5	0.82	-0.6	-3.1	94
16.0	0.88	-0.4	-2.4	71
16.5	0.94	-0.3	-1.8	48
17	0.96	-0.2	1.2	34
17.5	0.98	-0.1	-0.7	19

Table of Coefficients for Prediction of Adult Height for Girls

Age (years) ***Premenarche***	Coefficient for Height	Coefficient for Age	Coefficient for Bone Age	Constant
4-5	0.95	–6.5	0	93
6.0	0.95	–6.5	–0.4	93
6.5	0.95	–5.5	–0.8	93
7	0.94	–5.1	–1.0	94
7.5	0.93	–4.7	–1.1	94
8	0.92	–4.4	–1.5	95
8.5	0.92	–4.0	–1.9	96
9.0	0.92	–3.8	–2.3	99
9.5	0.91	–3.6	–2.7	102
10	0.89	–3.2	–3.2	106
10.5	0.87	–2.7	–3.6	109
11.0	0.83	–2.6	–3.6	114
11.5	0.82	–2.5	–3.6	115
12.0	0.83	–2.4	–3.4	111
12.5	0.83	–2.3	–3.3	108
13.0	0.85	–2.0	–3.1	98
13.5	0.87	–1.8	–3.0	90
14.0	0.91	–1.6	–2.8	79
14.5	0.99	–1.4	–2.5	67
Age (years) ***Postmenarche***	**Coefficient for Height**	**Coefficient for Age**	**Coefficient for Bone Age**	**Constant**
11.0	0.87	–2.3	–3.3	100
11.5	0.89	–1.9	–3.3	91
12.0	0.91	–1.4	–3.2	82
12.5	0.93	–1.0	–2.7	67
13.0	0.95	–0.9	–2.2	55
13.5	0.96	–0.9	–1.8	48
14.0	0.96	–0.8	–1.4	40
14.5	0.97	–0.8	–1.3	37
15.0	0.98	–0.6	–1.1	30
15.0	0.99	–0.4	–0.7	20

Appendix E

SURVEY ON THE USABILITY OF AN AUTOMATED SYSTEM FOR BONE AGE ASSESSMENT USING HAND AND CLAVICLE BONES

This survey is part of a study to evaluate the usability of bone age assessment system. You were specially selected as you have knowledge in this area. By replying to the survey, you will be providing useful feedback on the performance of the system.

The assessment of skeletal maturity or bone age has an important role in diagnostic and therapeutic investigations of growth disorders or genetic problems in children and young adults. This research is developing an automated system for bone age assessment using the hand and clavicle (BAASHC).

The main aim of an automated system for BAA is to eliminate the observer variability and save time and manpower in bone age assessment. This research adopts a novel approach because the images of both hand and clavicle bones are used for BAA. The system uses the X-ray images. The approach gives higher accuracy and more reliable decision is made in BAA. This approach also overcomes problems faced in forensic cases that are presented with missing or noisy information of the hand.

This system for bone age assessment could be used in both clinical and research environments and in forensic science.

Thank you for your cooperation.

Yours Sincerely,

Marjan Mansourvar
PhD Candidate
Department of Information System
Faculty of Computer Science and Information Technology (FCSIT)
University of Malaya (UM)
Marjan2012@siswa.um.edu.my

Section A: General Information

1) Name

2) Profession

3) Gender

Male ☐ Female ☐

Section B: Usability Evaluation of System

In the following questions, please indicate your opinions concerning the usability of system, by ticking (√) in the relevant box using a 5-point Likert-like **(1 --- 'STRONGLY DISAGREE' and 5 --- 'STRONGLY AGREE')**.

No.	Statements					
	Affect	Strongly Disagree <-> Strongly Agree				
		1	2	3	4	5
A1	Working with this system is satisfying					
A2	I would recommend this system for BAA to my colleagues					
A3	I enjoyed my sessions with this system					
A4	Sometimes I don't understand the way the system behaves.					
	Efficiency	Strongly Disagree <-> Strongly Agree				
B1	The automated BAA system helped me to overcome the problems that I had faced with the manual BAA method					
B2	Using this system saves time					
B3	Using this system saves manpower					
B4	The system is presented attractively					

	Helpfulness	Strongly Disagree <-> Strongly Agree				
C1	Using the hand and clavicle bones is helpful in bone age assessment					
C2	I can work with the automated system for BAA					
	Control	Strongly Disagree <-> Strongly Agree				
D1	It is easy to work with the system even as a non-specialist person.					
D2	The system is inconsistent					
D3	The speed of the system is appropriate					
D4	I can understand at a glance what are the options available in each menu.					
	Learnability	Strongly Disagree <-> Strongly Agree				
E1	It takes too long to learn the functions of the system					
E2	It is easy to make the BAA system do what I want					
E3	Overall, the system is useful for BAA					
E4	I can remember easily how the BAA system work					

Do you have any comments to improve the system?

____

____

******** Thank you for your participation ********

Appendix F

UNIVERSITI MALAYA
PUSAT PERUBATAN UM

JAWATANKUASA ETIKA PERUBATAN
PUSAT PERUBATAN UNIVERSITI MALAYA
ALAMAT: LEMBAH PANTAI, 59100 KUALA LUMPUR, MALAYSIA

Permohonan Menjalankan Projek Penyelidikan

(Application to Conduct Research Project)

1. Tajuk projek (Project title): Development an automated system for bone age assessment using X-ray images.

2. Penyiasat utama (Principal investigator):

2.1 Nama (Name): Marjan Mansourvar

2.2 Jawatan (Designation): Faculty of Computer Science and Information Technology (FCSIT)

2.3 Jabatan (Department): Information System

2.4 E-mel (E-mail): marjan136285@gmail.com

3. Penyiasat-penyiasat lain (Other investigators):

Nama (Name)	Jawatan & Jabatan	Tandatangan/Cop
Sameem Abdul Kareem	FCSIT	
Maizatul Akmar Ismail	FCSIT	
Ram Gopal Raj	FCSIT	
Fariza H. Nasaruddin	FCSIT	

4. Keadaan projek, jika berkenaan (Project status, if applicable):

4.1 Projek ini adalah projek (This project is)

BA Baru (New)   Sambungan (Continuation)

4.2 Jika sambungan, sila beri butir-butir berikut:
(If it is a continuation project, please give details as follows):

a. Tajuk asas projek (jika berlainan):
(Initial project title [if applicable])

b. Tarikh bermula (Date of commencement):

c. Tarikh akan siap (Date of completion): 2014

d. Bantuan diterima dahulu dari (Previous sponsorship):

e. Jumlah bantuan yang telah diterima (Amount of sponsorship):

5 . Nyatakan jika projek ini adalah sebahagian keperluan pengajaran ijazah/lepasan ijazah
(Please state whether this project is for fulfillment of basic/postgraduate degree)

5.1 Ya/Yes
(Nyatakan pengkhususan ijazah, samada Sarjana Muda, Sarjana atau PhD /
State name of degree, e.g Bachelor, Master or PhD): PhD

5.2 Tidak/No

6. Geran untuk kajian (Nyatakan sumber geran) / Research funding (State source of funding)

6.1 Tiada geran / No funding Tiada geran diperlukan / No funding needed

Untuk dimohon kemudian / To apply later

6.2 Penaja kajian / Trial sponsor - Nyatakan nama penaja / State name of sponsor

____

6.3 Geran kajian / Research fund - Nama geran kajian / Name of fund/research vote

This research is supported by Flagship Research Grant FL012/2012, University of Malaya (UM).

7. Maklumat projek / *Project information*

7.1 Latar belakang, bahan-bahan rujukan dan rasional yang berkaitan dengan projek ini

(Background, literature reference and rationale for this project)

BAA is a skill in forensic science defined as Forensic Age Estimation (FAE) for the purpose of providing the most accurate value for the chronological age (CA) of an unknown subject in criminal investigations (Paewinsky et al., 2005). The expression of estimation is explained more clearly than other terms for diagnosis, and shows the main limitations in this skill. Forensic Age Estimation is not an introduction to a new field of skill in forensic science and judiciary history, as the eruption of the second molar was used in the Roman Empire as an indicator for calling young males for military service (Schmeling, 2008). In the nineteenth-century, age was estimated by dentists, and tooth eruption was considered to be a reliable method to detect the age of a child. In that era, the minimum criminal age was calculated to be 7 years old in Britain. However, some experts have objected to this method for the estimation of age. In 1846, Dr Pedro Mata expressed his concern about estimating age based only on tooth eruption (Bandelt et al., 2001). Rontgen discovered X-rays in 1985 and his discovery triggered a revolution in the estimation of age for living subjects (Mould, 1995). This innovation, based on radiography of the skeleton, was used as a complement to tooth eruption in forensic practice. In 1886, Angerer was the first person who stated that the carpus bone in the hand is an indicator for the estimation of age in young people (Brothwell, 1981). The researchers tried to define the age of the subject based on the radiologically defined maturation of the human skeleton. Between 1950 and 1980, the most important methods for the estimation of age based on radiological analysis of the carpus bone were defined as Greulich and Pyle (GP), and Tanner and Whitehouse (TW) methods (Greulich & Pyle, 1959). There are many disadvantages concerning the accuracy of these traditional BAA methods. Firstly, the manual approaches in BAA are prone to the observer's variability and this issue decreases the accuracy of bone age assessment at the stage of development. Secondly, bone age assessment using these methods are largely limited to subjective decisions, meaning that assessment using these methods is dependent on the experience of the radiologists or doctors who assess the bone. Thirdly, these manual approaches are very time-consuming. (Bilgili et al.,2003). As a result, there is pressing need to develop an automated method for bone age assessment.

7.3 Keputusan-keputusan yang dianggapkan, jika ada (Expected outcome, if any)

The expected output of this study will be an automated web-based system for bone age assessment based on the X-ray images, for human identification purpose.

7.4 Kepentingan dan/atau kegunaan lanjut, jika ada (Significance and/or further practical applications, if any).

Bone age assessment (BAA) has been a subject of great academic interest for a long time. The procedure is regularly carried out on children and juvenile for evaluating growth, management of limb length discrepancies, management of scoliosis, and the diagnosis of endocrine disorders and genetic disorders. The traditional methods that had been used to determine age are often not accurate. Hence, there is a growing demand for automated methods for determining an individual age with more accurate results (Mansourvar et al., 2013).

It is expected that an automated system would improve the accuracy of bone age assessment in both clinical practices and in medical research. The use of an automated system would decrease the costs of estimation bone age as a result of the time saved and the less manpower needed.

The manual methods have drawbacks because observations can be subjective. An automated system, on the other hand, would eliminate the observer's variability and also benefit from the intervention by experts to be more effective and accurate in the assessment of bone age.

7.5 Jadual waktu bagi projek ini, termasuk tarikh bermula, fasa-fasa dalamnya dan tarikh selesai

(Time frame for project, including duration, phases, start date and end date estimates)

1 year: from Sep. 2012 to Sep. 2013

Title	INTELLIGENT FORENSIC SYSTEM
Project No	FL012-2011
SAGA No	5659962
Project Leader	1. Sameem binti Abdul Kareem (Current)
Faculty	Fakulti Sains Komputer & Teknologi Maklumat
Department	Jabatan Kepintaran Buatan
Start Date	22/12/11
End Date	21/12/14
Project Status	New

8. Methodologi/kaedah yang dicadangkan / Proposed methodology

8.1 Rekabentuk projek (Sila sertakan nota keterangan/apendiks jika perlu)
Study design (Please submit explanatory notes/appendices if necessary)

Sila beri butir-butir mengenai populasi atau bahan-bahan yang akan disiasat, prosedur-prosedur, cara-cara memproses data dan sebagainya. (Please give details concerning population or materials to be studied, procedures, and data processing methods etc)

The research methodology is implemented in seven steps, as follows:

- A review of the literature pertaining to BAA ;
- Observational study;
- A questionnaire survey to investigate the current methods for BAA used in University of Malaya Medical Centre (UMMC);
- Interviews with experts in radiology and Orthopaedic surgery pertaining to BAA;
- Analysis of collected data and results;
- Design and implementation of the BAA system;
- Evaluation of the accuracy and usefulness of the BAA system

8.2 Teknik pengumpulan data yang digunakan / Data collection technique involved:

Prospektif / Prospective

Retrospektif / Retrospective

Lain-lain (Sila nyatakan) / other technique (Please specify):

____

This research will develop a computerized system for bone age assessment.
At the first for developing it needs the X-ray images for the knowledgebase, and then at the end it needs collaboration a radiologist for humanity test and evaluation the accuracy of the system.
(The X-ray images for the past (the available images) is enough for this research.

8.3 Adalah subjek bernyawa terlibat? / Are human subjects involved?

Ya / Yes

Sila pilih / Please Select:

Pesakit/Patients (Sila nyatakan jumlah pesakit yang terlibat/Please state number of patients involved)

____

Sukarelawan/Volunteers or Normal controls

Kaji selidik kumpulan sasaran (Sila lampirkan Borang Kaji Selidik) / Survey of target groups (Please attach questionnaire)

Tidak / No

8.4 Adakah terdapat kaedah terapeutik/dadah baru diuji? / Are new therapeutic procedures/drugs being tested?

Ya / Yes

Nyatakan prosedur/dadah yang digunakan (State the procedures/drugs used)

Tidak / No [redacted]

8.5 Adakah prosedur yang mengganggu terlibat /Are invasive procedure applied?

Ya/ Yes

Sila nyatakan prosedur / State the procedures

Tidak / No [redacted]

8.6 Adakah terdapat sumber/peralatan yang akan digunakan di FPUM atau PPUM? Jika ya, sila senaraikan
(Will resources/ equipment in FOM or UMMC be utilized? If yes, please state)

Ya / Yes

X-ray images for database [redacted]

Tidak / No

9. Isu Etika / Ethical Issues

9.1 Adakah projek ini mematuhi prinsip-prinsip “Declaration of Helsinki”/garis panduan Malaysian Good Clinical Practice (GCP)

Does this project conform to the Declaration of Helsinki/Malaysian Good Clinical Practice (GCP) Guidelines?

Ya / Yes

Tidak / No

9.2 Apakah faedah kepada subjek di dalam projek ini?

(What are the benefits to research subjects of this study?)

This research will develop an automated system to assess subject age based on the bone image. The method could be implemented in any law enforcement agencies to assessment of age.

9.3 Apakah risiko kepada subjek di dalam projek ini?

(What are the risks to the research subjects of this study?)

None.

9.4 Bagaimanakah perlindungan untuk Serious Adverse Events (SAEs) (contoh: insurans, pembayaran, dll) disediakan?

(How is coverage for Serious Adverse Events (SAEs) (eg: insurance, payment, etc) provided for?)

Not Applicable

9.5. Adakah rawatan bermanfaat masih diberikan kepada subjek selepas projek ini selesai? Jika tidak, sila nyatakan sebab.
(Will beneficial treatment still be provided for research subjects after completion of the study? If no, please state why)

Ya / Yes

Tidak / No

Not Applicable

9.6 Adakah maklumat dan keizinan pesakit akan disediakan? / Will information to the patient and informed consent be provided?

Ya (sila isikan Borang Maklumat Pesakit dan Borang Keizinan Pesakit yang disediakan)
Yes (please fill in Patient Information Sheet and Consent Form provided)

Tidak / No

9.7 Adakah perbelanjaan projek ini dikenakan kepada subjek? Jika ya, sila nyatakan jumlah perbelanjaan yang terlibat. Jika tidak, siapakah yang akan menanggung perbelanjaan bagi kajian ini?

(Are expenses borne by the research subjects? If yes, please state the expenses incurred. If no, how are expenses provided for?)

Ya/Yes

Tidak/No

9.8 Adakah terdapat sebarang bentuk bayaran ditawarkan kepada subjek? Jika ada, berapakah jumlahnya?

(Will any form of payment be offered to research subjects? If yes, what is the amount?)

Ya/Yes

Tidak/No

10. Butir-butir lain *(Other information)*

This research aims to develop an automated system for bone age assessment using both images of the hand and the clavicle.

11. Ulasan Dan Kebenaran Ketua Jabatan/Unit/Makmal Terlibat (Comments and permission of relevant Head of Department/Laboratory)

Sila tandakan [□] (Please tick [□]): Tandatangan & Cop/Tarikh (Signature & Stamp/Date)

Jabatan Anatomi
(Department of Anatomy)

Jabatan Anestesiologi
(Department of Anaesthesiology)

Jabatan Farmakologi
(Department of Pharmacology)

Jabatan Farmasi, FPUM
(Department of Pharmacy, FOM)

Jabatan Farmasi, PPUM
(Department of Pharmacy, UMMC)

Jabatan Fisiologi
(Department of Physiology)

Jabatan Oftalmologi
(Department of Ophthalmology)

Jabatan Obstetrik & Ginekologi
(Department of Obstetrics & Gynaecology)
Jabatan Otorhinolaringologi
(Department of Otorhinolaryngology)

Jabatan Parasitologi
(Department of Parasitology)

Jabatan Patologi
(Department of Pathology)

Jabatan Pediatrik
(Department of Paediatrics)

Jabatan Pengimejan Bio-perubatan
(Department of Biomeical Imaging) [redacted]

Jabatan Perubatan Mikrobiologi
Department of Medical Microbiology

Tandatangan Pemohon (Signature of Applicant)

____________Sep. 2012___

______Marjan Mansourvar__

Tandatangan (Signature)

Marjan Mansourvar

13. Komen-komen Ketua Jabatan Pemohon (Comments of Head of Department)

Projek ini disokong/Tidak disokong (Support/Not supported)

--Sep 2012-- __Dr. Maizatul Akmar Ismail __

Tarikh (Date) Tandatangan & Cop Ketua Jabatan

(Signature & Stamp of Head of Department)

BK-MDU-002-E02